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CEREBRO-SPINAL FEVER

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CEREBRO-SPINAL FEVER

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THIS BOOK IS DEDICATED TO MY FRIEND
AND COLLEAGUE

MERVYN H. GORDON

AS A TRIBUTE TO THE GENIUS WHICH
CHARACTERIZES HIS RESEARCHES
IN BACTERIOLOGY

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PREFACE

THE winter of 1914–15 and the spring of 1915 have seen many more cases of cerebro-spinal fever in England than at any other time since the disease has been recognized. A large number of practitioners to whom cerebro-spinal fever had hitherto been little more than a name, or to whom the rare appearance of a sporadic case sufficed only to stimulate a temporary interest in the disease, found themselves ill-prepared to meet the mild but widespread epidemic which accompanied the concentration of troops at various centres of this country. This was inevitable, not only because cerebro-spinal fever was a new experience, but also because there was no manual published in this country to which reference might be made for guidance. This being so, an English monograph giving an account of the disease, its diagnosis, and its treatment, in so far as present knowledge admits of their presentation, seems to require no apology. As to the matter of the book, an effort has been made to cut down in length all discussions upon points which, however important, are still under investigation—and there are several such points in connexion with a disease which constantly reveals new phases even to those who have had exceptional facilities for observation.

As the book is primarily intended for use in actual practice, only those pathological facts are introduced which are necessary to the understanding of the subject. It is hoped that the deliberate inclusion of detailed instructions in the chapters dealing with lumbar puncture and treatment will be of service to those who are not already well acquainted with these matters.

My thanks are due to Dr. M. H. Gordon for his kind revision of Chapter III, to Dr. Archibald Leitch for several valuable criticisms made after reading the proof-sheets, and to Dr. W. Cunnington and Dr. L. Wilkinson for their help with the analysis of a large number of case-notes. For the references to certain cases of special interest under the care of other physicians grateful acknowledgements are made in the text. In similar fashion, when statements of fact or of opinion have been extracted from the literature of the subject, the author's name has invariably been given. A word of appreciation is due to the publishers for their prompt assistance in many matters connected with the production of the book.

THOMAS J. HORDER.

LONDON,
July 1915.

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CEREBRO-SPINAL FEVER

CHAPTER I

DEFINITION. NOMENCLATURE. HISTORY

§ 1. **Definition.**—A specific disease, due to infection of the body by the meningococcus, occurring both in epidemic and in sporadic form, and most often manifesting itself as an acute meningitis tending to involve the whole cerebro-spinal axis.

§ 2. **Nomenclature.**—The name here chosen seems least open to objection. 'Cerebro-spinal meningitis' is the best alternative, but cerebro-spinal meningitis may be caused by other micro-organisms than the meningococcus, and meningitis may not be present at all, or may not constitute the chief lesion, in some cases of meningococcus infection. 'Epidemic cerebro-spinal meningitis' is much less desirable because it suggests that there is an essential difference between the epidemic and the sporadic cases of meningococcus infection, which difference does not in fact exist. 'Meningococcus infection' brings the various pathogenic possibilities of the micro-organism into line with those of the pneumococcus, with which it has close analogies, but the term does not connote a disease.

But just as ‘ pneumonia ’ is used to express what is by far the commonest disease-process caused by the pneumococcus, so ‘ cerebro-spinal fever ’ is justified because it expresses the disease-process most commonly caused by the meningococcus. ‘ Cerebro-spinal fever ’ connotes an acute specific disease, which is what we want to convey by the name.

§ 3. **History.**—Glimpses of the disease, in its epidemic form, are caught in the literature of the Middle Ages. The first epidemic to be duly noted, however, occurred at Geneva in 1805. Not only were the main clinical features, as we now know them, described by Vieusseux, but a fairly adequate account of the post-mortem findings was also given by Mathey. A year later an outbreak of the disease occurred at Medfield in Massachusetts, and America has never been free for many years at a time from then until now. The Medfield epidemic was described by Danielson and Mann, who also verified the condition post mortem. Between 1806 and 1830 the disease showed itself in epidemic form in several others of the States. It was the study of one of these epidemics which led Elisha North to write ‘ A Treatise on a Malignant Epidemic commonly called Spotted Fever ’ (1811). During this same period the disease was rife in Europe also. In 1806–7 it broke out in the Prussian army, amongst the Spanish prisoners at Brianca, at Brest in 1813, and at Paris in 1814. These epidemics coincided with several outbreaks of typhus fever with which the cases of cerebro-spinal fever were to a certain extent confounded.

Between 1837 and 1850 a very widespread epidemic appeared in France, the disease being carried from place to place by the transfer of troops. The cases began amongst the civilian population in the south of France. They then appeared amongst the soldiers at the Bayonne and Dax garrisons. The 18th regiment, stationed in this region, developed cases of the disease, and for a period of four years the troops carried the infection to a large number of centres, at each of which a series of cases occurred—Bordeaux, Rochefort, Versailles, Chartres, Metz, Nancy, and Strasburg. By the year 1850 most of the large barrack towns of France had developed cases of the disease. These years (1837–50) also saw an epidemic in Italy, and the spread of the infection across the Mediterranean to Algiers. Gibraltar, Denmark, and Ireland also suffered. In America there were several fresh epidemics in various States, including the negro quarter of New Orleans.

The years 1851–61 included a large epidemic in Norway and Sweden. The disease spread from south to north of Sweden, ravaged the population from January to June, then subsided, to reappear in the following January at the spot where it ceased the year previously. In the seven years during which the disease raged it caused no less than 4,138 deaths in Sweden, where only two provinces out of twenty-four, and those the most northerly, escaped.

About the year 1861 the disease became much more widespread than ever before, many districts suffering which had hitherto been free. Various parts of

Germany suffered, especially Silesia. The disease also appeared in Hungary and Russia. Ireland suffered badly in 1865–8. In the United States the disease attacked the army of the Potomac in the winter of 1861–2, New York in 1863–6, and several other States and cities. It also appeared in the military school at Newport, R.I.

For a few years following 1870 the disease scarcely appeared in epidemic form, but in 1885–6 a recrudescence occurred in France, Italy, Germany, Austria and Scandinavia. This revival of cases in epidemic form gave the material for the bacteriological research which led Weichselbaum to make his discovery of the causative micro-organism in 1887. Leichtenstern and Bonome also contributed important facts in connexion with the pathology of the disease.

The years 1896–1903 saw fresh epidemics in most European countries, with a specially severe one in Portugal affecting more than 3,000 persons. This epidemic was studied fully by Bettencourt and França. In the United States the epidemics of this period led to researches by Flexner, Barker, Councilman, Mallory, and Wright.

During the past ten years (1905–15) there has been a revival of the disease in epidemic form over a very large area. This revival of cases appears to have started by the large outbreak which occurred in the United States in 1904. New York suffered heavily, the year 1905 showing no fewer than 2,755 cases. Two years later an almost equally severe outbreak occurred at Glasgow, at Edinburgh, and at Belfast, giving Scottish and Irish observers ample opportunities for investigation and popularizing, to a large extent, the study of the disease in Great Britain.

The New York epidemic gave Flexner full scope for trial of the serum manufactured according to his method and tested on monkeys. This serum was also tried thoroughly by Robb at Belfast and by Ker at Edinburgh. Many important contributions appeared in the literature of the subject, and the Report of the Rockefeller Institute went far to establish definitely the efficacy of the specific treatment. Still more recent epidemics in Europe offered similar opportunities there of testing the sera of Kolle and Wassermann, Jochmann, Ruppel, and others. This period in the history of the disease produced important bacteriological researches, establishing beyond reasonable doubt the causative nature of Weichselbaum's coccus and completing our knowledge of its cultural and biochemical characters (Lingelsheim, Gordon, Netter, and others). The same period also saw the evolution of the doctrine of 'the carrier', a doctrine which affords the most satisfactory solution of the problem of dissemination of the disease. This doctrine was elaborated by Dopter in France, by Bolduan and Goodwin in America, and by Arkwright in England.

The most recent experiences of the disease are those of the present epidemics in England and in France, now under thorough investigation and treatment (1915). At various barracks and camps the disease has appeared, and, as usual, the armies in the field have almost entirely escaped. Civilians also have suffered, a good deal of evidence going to show that some of the soldiers have acted as carriers whilst in billets. The coincidence of a severe epidemic of measles has contributed an additional catarrhal factor in connexion with the epidemiology of the present outbreak of cerebro-spinal fever.

CHAPTER II

EPIDEMIOLOGY. MODES OF DISSEMINATION

EPIDEMIOLOGY

§ 1. **General Characters of the Epidemics.**—Epidemics of cerebro-spinal fever are marked by several features peculiar to the disease, offering a striking contrast with other epidemic diseases. For a long time these features were very difficult of explanation, until the existence of 'carriers' became recognized, and supplied the solution to much of the epidemiological problem. Amongst these curious features may be mentioned the erratic nature of the outbreaks, the inability to trace the connexion between one epidemic and another, the relative or even total escape of certain localities close to others in which the disease was rife, and the small proportion of persons affected in any one district.

§ 2. **The Influence of Sporadic Cases.**—On clinical and on bacteriological grounds there is no distinction to be drawn between sporadic and epidemic cases of cerebro-spinal fever. Nor is there any real distinction epidemiologically. It is found that there is often a gradual increase of the sporadic cases immediately prior to an epidemic, and that there is a higher incidence of sporadic cases just after an epidemic has occurred. It is also noticeable that the number of cases of the disease that are not of the post-basic kind —the form most often met with amongst the sporadic cases—increases just before an epidemic and remains more frequent just after an epidemic. It is obvious that the relation between the sporadic and epidemic cases is very close. It is not entirely by means of the sporadic cases that the infecting agent persists, as will be shown, but there is little doubt that from the sporadic cases, as from a smouldering infection, new epidemics light up. The present conception of the disease, therefore, from an epidemiological point of view, is that of a very widespread infection, with a total morbidity that is very low, but with foci of more intense virulence here and there. These foci of more intense virulence appear and disappear, being preceded and followed by a somewhat higher level of permanent incidence in the districts concerned.

§ 3. **Geographical Distribution ; Seasonal Incidence.** —The geographical distribution of the disease is very wide, world-wide in fact. A certain affinity is shown for the north temperate zone. The countries that have suffered most have been those of Central Europe and the NE. States of America.

Epidemics of cerebro-spinal fever show a very striking seasonal incidence. *Epidemic cerebro-spinal meningitis is a disease of winter and spring.* In Germany four-fifths of all the cases recorded in the four successive years 1905–8 occurred in the spring and winter months (Netter and Debré). This seasonal incidence is borne out by all observers and is a very important feature of the disease. It compares markedly with the seasonal incidence of poliomyelitis epidemics, which are at their height in the summer months. There is apparently an increased virulence of the meningococcus during the cold months of the year, or else the frequency of catarrhal affections at this period makes for greater diffusibility of the micro-organism.

§ 4. **Age ; Sex ; Occupation ; Hygienic Conditions.**—*Age* is another important factor. The incidence amongst infants is very high in nearly all epidemics ; it is great amongst children, less so in adolescents, and least in persons above middle age. Though uncommon, it does occur in the elderly. In the German epidemic already referred to over 80 per cent of the cases occurred in persons under sixteen years of age. In the New York epidemics of 1905–7, out of 4,000 cases, 67 per cent occurred in children under ten years of age. *Sex* has no influence upon the incidence of the disease. *Occupation*, however, is an ætiological factor of importance—chiefly in relation to soldiers, amongst whom the disease is relatively very common. Netter and Debré speak of epidemic cerebro-spinal meningitis as being a disease especially ‘ of infants and soldiers ’. The soldiers who suffer are those living in barracks and garrison towns, not those in the field. Overcrowding is the hygienic factor most often blamed for the special incidence amongst the military population. Miners have been specially affected in some of the epidemics, a fact attributed by

Jehle to the prevalence of pharyngeal catarrh amongst this class of workers.

§ 5. **Influence of Other Infective Processes.**—Epidemics of cerebro-spinal fever are prone to coincide in time with recrudescences of influenza, pneumonia, measles, and scarlet fever. It is doubtful if this is more than a fortuitous observation. The naso-pharynx is liable to catarrhal inflammation in all these diseases, and pneumonia and influenza have the same seasonal incidence as cerebro-spinal fever.

§ 6. **The Contagiousness of the Disease.**—The question whether or no cerebro-spinal fever is contagious has been a matter of much dispute. The facts would appear to be these—that the disease is contagious, but that the degree to which it is so is very slight. Out of 2,000 houses implicated in an epidemic less than 7 per cent furnished more than one case of the disease (Arkwright). The proofs of the contagiousness of the disease are, briefly, these: (i) the occasional transmission of the disease to doctors and nurses; (ii) the occurrence of a succession of cases in one family and in the same house; (iii) the importation of the disease into a new country or locality; (iv) the mode of spread in any locality; (v) the immunity enjoyed by collections of persons living under the same conditions as those affected by the disease, but unable for some reason to come into contact with them (Netter and Debré). Although direct contagion is uncommon, plenty of authentic instances of its occurrence have been reported. Sewall, in the New York epidemic in 1872, observed that six members of one family contracted the disease successively, at intervals of one to thirty-four days. Leichtenstern relates an instance where three nurses and a sister in charge of cases of cerebro-spinal fever contracted the disease; three of these four nurses had not left the hospital for some time and therefore were not able to contract the disease outside. Mention has already been made (Chap. I, § 3) of the remarkable transference of the disease to various towns in France by the 18th regiment of the French army during thirteen years.

Modes of Dissemination

§ 7. **The Naso-pharynx as the Habitat of the Meningococcus.**—Until the discovery of the meningococcus in the naso-pharynx of patients suffering from cerebro-spinal fever no rational explanation of the mode of dissemination of the disease was forthcoming. Several observers reported the presence of the coccus in this situation in meningitic patients, but no great significance attached to the discovery until Albrecht and Shon, in 1901, proved that the coccus was almost invariably found, provided the investigation were made sufficiently early in the disease. v. Lingelsheim, taking into account the low degree of vitality of the coccus outside the body, and employing the necessary precautions to ensure its growth, obtained evidence of the presence of the coccus in over 66 per cent of cases examined. Netter and Debré obtained a still higher percentage of positive results. But the coccus was found to leave the naso-pharynx during the later stages of the disease. The figures obtained by the last-named workers were as follows :

Stage of the disease.	*Percentage of positive results.*
First week	78·55
Second week	60·0
Third week	50·0
Fourth week	25·0
After fourth week	15·35

In patients examined during the first three days of the disease the percentage of positive results has been estimated at more than 90 per cent.

The *site of election* of the coccus in the upper respiratory tract is very precise. Although it is occasionally found in the fauces, and even in the saliva, *its exact habitat is the upper part of the naso-pharynx and the posterior nares.* The earlier bacteriological investigations, made in ignorance of this special distribution of the coccus, are now to be disregarded. Similarly, in dealing with suspected cases of the disease, or in examining contacts for the meningococcus—a very important routine investigation in times of epidemics—a different method is now employed from what was formerly in use. Instead of dealing with the nasal mucus, material is obtained from the roof of the naso-pharyngeal wall, and cultures are made straightway on to suitable media (see Chap. III, § 3). Fig. 1 shows the anatomical relations of the parts and of the swab that is passed through the mouth to the infected region. In the great majority of cases of cerebro-spinal fever there is very little difficulty in obtaining the meningococcus from this region if the patient be examined early and by this particular method. A special swab, used for this purpose, is illustrated in Fig. 2.

§ 8. **Meningococcus ' Carriers '.**—But the spread of an epidemic of cerebro-spinal fever is not explained by the discovery of the coccus in the naso-pharynx of actual patients; for, as already seen, the disease rarely spreads by direct contact from patient to patient. This difficulty was solved when Albrecht and Shon found that the coccus could be isolated from the naso-pharynx of healthy persons living in epidemic zones. In other words, they isolated the meningococcus from healthy contacts. This

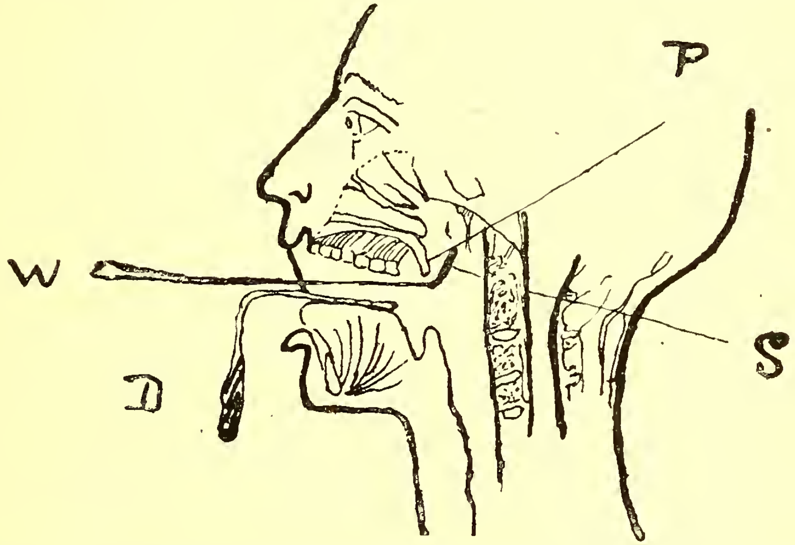

FIG. 1.—Diagram illustrating the method of taking material from the naso-pharynx by means of a special swab. W = wire holder of S = swab, P = soft palate, D = tongue depressor. (After Dopter.)

discovery led to many investigations along similar lines, with the general result of establishing the fact that for every case of cerebro-spinal fever there exist, in times of epidemic, a number of healthy carriers variously estimated at ten to thirty. Some authors give much higher figures than these.

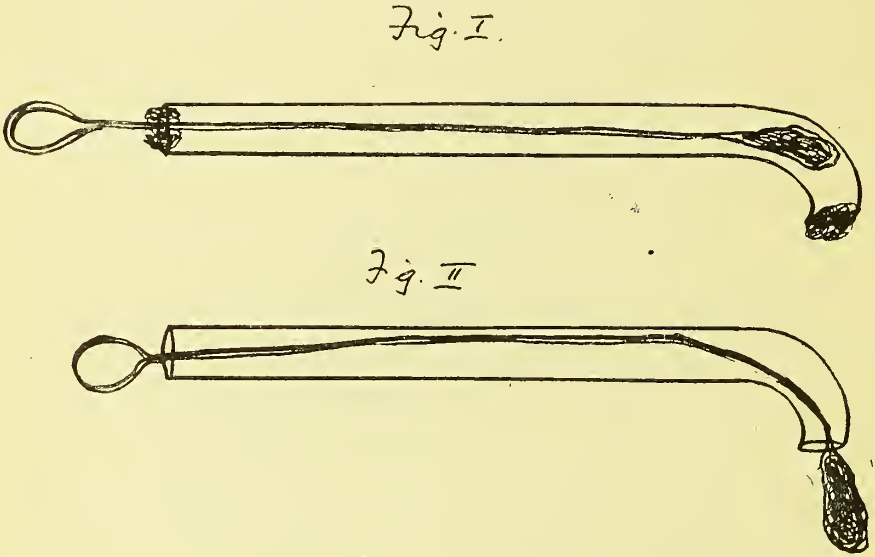

FIG. 2.—Diagrams illustrating special swab (West's) used for taking material from the naso-pharynx. In Fig. I the flexible wire holding the swab is contained within the bent glass tube. In Fig. II it is extruded as in use. The swab is here reduced one-half in size.

The number of carriers varies with several inconstant factors. (i) There is a seasonal incidence for carriers, as there is for cases: Netter and Debré found twice as many carriers in the spring months as in the summer months. (ii) The number of carriers varies also with the stage, and with the character, of the epidemic: there are more carriers when the epidemic is fully developed than during the waxing and waning stages, and there are also more carriers when an epidemic is severe than when it is mild. (iii) The closeness of contact between the individuals affects the number of carriers: mothers who nurse their meningitic infants are found to be carriers almost invariably,[1] and carriers are particularly abundant in schools and in barracks.

§ 9. **The Degree of Persistence of the Meningococcus in the Naso-pharynx.**—The naso-pharynx of the meningitic patient is usually free from the coccus in three or four weeks after convalescence begins—very often it is free long before this. The estimation of the duration of the coccus in the naso-pharynx of carriers is a much more difficult matter. It is probable that here, also, the naso-pharynx is free in three or four weeks from the time of contact. But there is increasing evidence that in some cases the coccus persists for a much longer period than this—even up to several months. According to some authors carriers may show a periodicity, the coccus appearing and disappearing.

Although the existence of *permanent carriers* has perhaps not been definitely proved, it seems highly probable that such persons exist, and that they harbour the meningococcus in the naso-pharynx just as other persons harbour *B. typhosus* in their intestinal tract. If such be the case it is clear that there is here a rational theory of the epidemiology of cerebro-spinal fever.

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[1] Following the general rule, that the flora of the naso-pharynx of infants and of their mothers are usually identical.

§ 10. **Theory of the Epidemiology of Cerebro-spinal Fever.**—An epidemic of the disease is due to the increase in virulence and to the spread of the meningococcus present in the naso-pharynx of the sporadic carrier. The determining factors in this dissemination are chiefly cold, the crowding together of individuals, and the presence of catarrhal affections. The degree to which the meningococcus occurs in the naso-pharynx of healthy persons, not exposed to infections and not tested during an epidemic, is as yet unknown. The point is still under investigation. German observers found the coccus present in 1·73 per cent of 9,111 men examined in the Munich barracks under these conditions, but this figure may be higher than one obtained from a like number of individuals not so closely congregated, and not forming a community so disposed to the disease as is a garrison.

The actual mode of conveyance of the meningococcus from the carrier, whether healthy or not, to the unaffected person, is undoubtedly by means of those minute droplets of buccal secretion which accompany speech, coughing, sneezing, or kissing. The droplets are infected by the coccus in the mouth, and their passage through the air conveys the micro-organism to the mucous membrane of the contact. Contagion by means of dried sputa is much less likely owing to the low degree of viability of the coccus. Indeed, this latter fact speaks against all forms of indirect contagion, and speaks for the necessity of direct contact. The recipient of the coccus may, or may not, develop cerebro-spinal fever: most often he does not, for it is known that there are many more healthy carriers than actual cases of the disease. And it is the healthy carrier who is the danger rather than the convalescent carrier.

With the decline of an epidemic, and with the tendency for the meningococcus to die out, even in the naso-pharynx, the number of carriers rapidly declines, leaving, however, a few healthy persons as links between the old epidemic and a possible new one. In this connexion it must also be remembered that the sporadic cases of the disease are always with us, and that they alone would serve to keep alive the specific coccus of the epidemics.

CHAPTER III

THE MENINGOCOCCUS

ANTI-MENINGOCOCCUS SERUM

§ 1. **Morphology.**—The meningococcus belongs fundamentally to the staphylococcus group, as do all Gram-negative cocci. It is never found to form even short chains, provided this point be studied in connexion with growth of the coccus in broth (Gordon). When examined in tissues or in inflammatory exudates the coccus is seen chiefly as a diplococcus, but also as single cocci and as tetrads. The coccus is rather smaller than the M. catarrhalis and is larger than the gonococcus. When examined in preparations made from cultures, the diplococcal form is by no means so constant. Under high powers of the microscope the diplococci obtained from the tissues are seen to consist of a pair of hemi-ellipses with their flat surfaces placed together, a straighter line dividing them than is the case with the gonococcus,

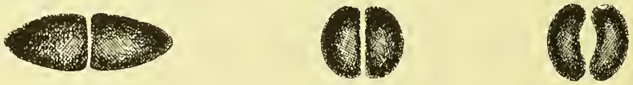

Fig. 3.—Illustrating the shape of individual members of pneumococci, meningococci, and gonococci respectively. These shapes are only seen in films prepared directly from exudates, not in films made from cultures.

the two members of which often show a slight tendency to be kidney-shaped. The individual members examined from culture preparations are usually spherical rather than elliptical and vary considerably in size.

§ 2. **Staining reactions.**—The meningococcus stains readily by all aniline dyes. It is invariably Gram-negative, a point of extreme diagnostic importance. If, as Gordon points out, care be taken to use controls (Staphylococcus aureus as a Gram-positive and B. coli as a Gram-negative micro-organism) in order to ensure proper working of the stain used, confusion never arises (Abel). Degenerate forms of the coccus occur readily on solid media, and these may not stain well.

§ 3. **Conditions of growth on artificial media.**—The meningococcus, on first being isolated from the body, requires the addition of some animal protein to ordinary media to ensure its growth. After cultivation for three or four generations, however, it will grow upon ordinary agar; but subcultures on this medium are apt to die rather suddenly. A very convenient medium for the first (and subsequent) growth is ascites agar or Wassermann's nutrose ascites agar (nasgar). Failing a stock of either of these, a little sterile fresh blood smeared upon an agar slope forms a most useful and certain medium.

The meningococcus is an *obligatory anærobe,* failing to grow in anærobic cultures.

As regards *temperature,* optimum growth takes place at 36°–37° C. It ceases at 42° C. and at

25° C. *Failure to grow below 25° C. is utilized as a most important point of distinction between the meningococcus and most other Gram-negative cocci occurring in association with it.*

The *appearance of colonies* of the meningococcus on ascites agar plates and slopes is another point of importance. *On plates* the colonies after twenty-four hours' growth at 37° C. appear as smooth, moist, grey, translucent, circular or oval discs with regular outline. Pigment is entirely absent. *On slopes* similar features are seen. The growth is always more abundant at the bottom of the slope, because the water of condensation favours it. In this condensation water there is uniform turbidity and some sediment of cocci.

The growth comes away readily from the medium, and if a portion of it is taken up on the platinum needle it is found to emulsify readily in a drop of water on a glass slide.

§ 4. **Vitality.**—Susceptibility of the meningococcus to *cooling* has been referred to already. The other condition to which it is highly sensitive is *drying*. Most observers agree that the coccus perishes rapidly under conditions of desiccation. *Sunlight* kills the meningococcus in a number of hours variously estimated by different workers as two to twelve.

Disinfectant solutions destroy the coccus readily. Flügge found it to be killed in one minute by a 3 per cent solution of peroxide of hydrogen, by a 1 per cent solution of carbolic acid, and by a 10 per cent solution of menthol. (Quoted by Heiman and Feldstein.)

Autolysis, to which the meningococcus readily tends, was shown by Flexner to be due to an intracellular enzyme.

§ 5. **Fermentation Powers.**—The meningococcus is able to ferment glucose and maltose but not saccharose.

§ 6. **Serum Reactions.**—(i) *Agglutination.* A great deal of painstaking work has been done in connexion with specific agglutinins for the meningococcus. But no very practical results have as yet been obtained. The difficulties are many. The fundamental nature of the micro-organism as a member of the staphylococcus group, with inherent tendencies to clumping, may account for much that is inconsistent in the results observed by various workers. One significant fact appears to have emerged from the experiments: the existence of different strains of the meningococcus differing in their serum reactions. An insight into the difficulties of this research may be had by realizing that the agglutinating action of a serum with the same strain of meningococcus varies from day to day; that there are group agglutinins; and that certain strains of the gonococcus are definitely agglutinated by meningococcus immune serum in dilutions which may not agglutinate the meningococcus itself. These difficulties have been more recently combated to a certain extent by the employment of 'absorption' methods,—following the principle that specific agglutinins are absorbed only by bacteria belonging to the same species as those used in the production of the immune serum. But even so there has not as yet evolved any method of practical diagnostic value, and the whole subject is still one for laboratory investigation.

(ii) *Fixation of Complement.* This reaction is probably much less specific than the agglutination reaction when dealing with a doubtful strain of the meningococcus.

§ 7. **Pathogenesis.**—The meningococcus is pathogenic for most animals. In *mice* and *guinea-pigs* subcutaneous injections of live cultures have little or no effect, but intraperitoneal inoculation leads to severe reaction and death in a few days. An intense purulent peritonitis is found post-mortem, with many intra- and extracellular diplococci in the exudate. Evidence of a general infection is forthcoming in the demonstration of the coccus in the spleen and in the heart's blood.

In rabbits very large doses of live meningococci given intravenously are often tolerated without acute symptoms. But a state of extreme emaciation often occurs with death after a prolonged interval (Horder and Gordon). In such a case it may be impossible to demonstrate or to cultivate the coccus from the animal after death, but the condition demonstrates the marked toxicity of the meningococcus.

In dogs and goats the injection of live cultures of the meningococcus into the pia-arachnoid space has led to fatal nervous symptoms, and occasionally the lesions of an acute meningitis have been demonstrable post mortem.

In monkeys all the characteristic changes brought about by the meningococcus in man have been produced by the intraspinal injection of large doses of living meningococci. Such lesions, with the acute symptoms produced by them, were first demonstrated by von Lingelsheim. A short time afterwards Flexner repeated these observations and also succeeded in reproducing the more chronic features of cerebro-spinal meningitis, associated with hydrocephalus, by the use of frequent small doses of the micro-organism.

§ 8. **Cocci resembling the Meningococcus.**—The above description refers throughout to the diplococcus of Weichselbaum, the recognized causative agent in cerebro-spinal fever. It is necessary to refer here to other Gram-negative cocci which have from time to time been isolated from the naso-pharynx in the course of the many investigations which have been undertaken during recent years. These investigations have demonstrated the existence of several groups of micro-organisms possessing somewhat similar features, but also possessing differential characters that are still being elaborated. These groups are as follows :

(i) Meningococcus (Weichselbaum).

(ii) Para-meningococcus (Dopter), a coccus which fails to agglutinate with the usual serum, but which possesses specific agglutinins and precipitins of its own. It has been isolated from a few cases of meningitis.

(iii) Diplococcus crassus (Jaeger), for some time confounded with Weichselbaum's coccus. It has been found as a secondary infection in the cerebro-spinal fluid from which the true meningococcus has also been isolated.

(iv) Chromogenic diplococci—flavus, cinereus, siccus (Lingelsheim), probably not pathogenic at all in respect of the meninges.

(v) Micrococcus catarrhalis (Pfeiffer).

(vi) Gonococcus (Neisser).

These micrococci show differential points with regard to cultural properties, fermentation powers, and serum reactions. In work done upon the flora of the naso-pharynx these differential points are of great importance, in order to determine accurately the existence of the true meningococcus carrier.

§ 9. **The Endotoxin.**—The toxic action of the meningococcus is exerted by means of an endotoxin. This follows from the fact that no soluble toxin forms in the culture media in which growth has taken place. This endotoxin is set free by the disintegration of the coccus as the result of the intracellular ferment already mentioned.

§ 10. **The Production of an Immune Serum.**—Beyond the mere demonstration of the fact that a serum possessing immune properties could be produced (Bonhoff and Lepierre, Jaeger, Kolle and Wassermann), nothing of practical value was done until, almost simultaneously in 1906, Jochmann in Germany and Flexner in America published their researches upon sera which they had proved to possess potent immune substances for use in actual cases of meningococcus meningitis. The credit of first suggesting the intraspinal use of the serum is due to Jochmann, though Flexner was the first to make extensive trial of this route.

§ 11. **Method of Preparation of the Serum.**—The horse is used by all workers and the general method of preparation is the same, with minor points of difference in technique. Flexner alternates injections of live cocci with injections of autolysed cocci, after immunization has proceeded to a certain point by the use of killed cultures ; the injections are made subcutaneously throughout. Jochmann follows the subcutaneous injections by intravenous injections when a certain degree of resistance has been established. In England the technique adopted at the Lister Institute and at the Wellcome laboratories is very similar to this.

The process of immunization of the horse is very slow ; serum withdrawn in less than six months from the beginning of the injections is not found to be very rich in antibodies. This slowness of immunization is compensated for by long retention of the immune substances once they are formed : one of Flexner's original horses was found to yield a very potent serum after the lapse of six years.

§ 12. **Nature of the Immune Substances.**—These are probably several in kind, but nothing is known definitely as to their relative importance in relation to the therapeutic action of the serum. There is 'test-tube' evidence that the serum contains bacteriolysins, i.e. substances possessing the power of disintegrating meningococci when the serum is brought into contact with them ; opsonins, i.e. substances capable of stimulating phagocytosis; and anti-endotoxins, i.e. substances having a neutralizing effect upon the specific toxin of the coccus. The serum has also been shown to contain agglutinins, precipitins, and complement-fixation bodies—substances that have no necessary relation to the therapeutic potency of the serum.

§ 13. **Standardization of the Serum.**—Despite many efforts in this direction, no satisfactory method of estimating the strength of the serum has yet been devised. Flexner and Jobling have attempted a method of standardization by determining the phagocytic activity induced by the serum. Kolle and Wassermann utilize the complement-fixation method.

§ 14. **Results of Serum Treatment.**—There is a consensus of opinion amongst practically all workers *who have had a large number of cases of the disease under their care,* that the serum lowers the mortality of the disease from about 80 per cent to 30 per cent, cuts short its course, and reduces the number of its complications and sequels. Like all other immune sera, it is of the utmost importance that the serum be administered early in the disease and in liberal amount. It must be given by the intraspinal route and not subcutaneously. Some strains of the meningococcus, no doubt, prove 'fast' in regard to the serum; if experience of a particular brand of serum in an epidemic is disappointing, another brand should be tried, or, better still, cultures of the coccus concerned should be included amongst the strains used for immunization. (See also Chapters XII and XIII.)

CHAPTER IV

THE CEREBRO-SPINAL FLUID IN HEALTH AND DISEASE

§ 1. **Anatomy.**—The cerebro-spinal fluid bathes the whole of the brain and spinal cord. The fluid lies in the space bounded by two membranes—the pia mater, which closely invests the grey matter of the cerebro-spinal axis, and the arachnoid mater, which lies immediately beneath, and is closely attached to, the dura mater. The space containing the fluid is called the subarachnoid space or, perhaps more conveniently, the *pia-arachnoid space.* It is complex in its disposition at certain regions, simple at others. Thus, in the cranium it is expanded into various chambers termed *cisternæ,* the chief of which is the cisterna magna, lying over the wide interval between the back part of the under surface of the cerebellum and the bulb. The cisterna magna is continuous through the foramen magnum with the posterior part of the pia-arachnoid space of the cord. Two other important cisternæ are the cisterna pontis, which continues upwards on the floor of the cranium the anterior part of the spinal pia-arachnoid space; and the cisterna basalis, which lies in front of the pons. (See Fig. 4.) The pia-arachnoid space is seen in its simplest form in the region of the thoracic cord, where it provides an annular sheath, of small calibre, for the spinal axis.

There is an important prolongation of the pia-arachnoid space in the lumbo-sacral region, containing the filum terminale and the cauda equina. It is this part of the space which is tapped by a lumbar puncture, and it is into this cisterna that serum is inserted in the treatment of a case of meningococcus meningitis. (See Fig. 5.)

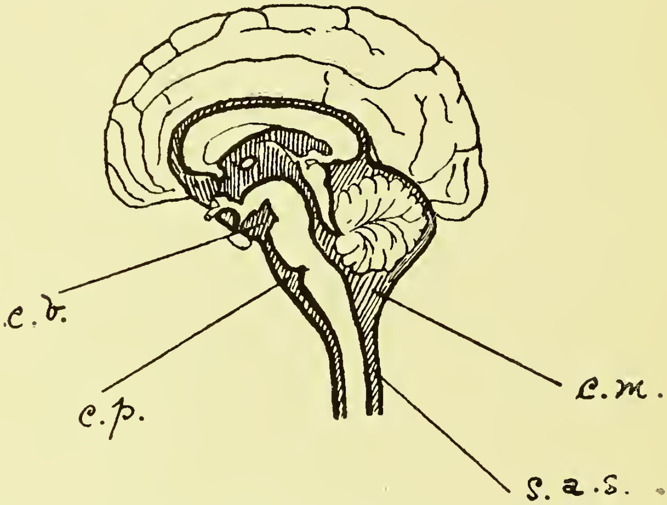

FIG. 4.—Showing the pia-arachnoid space and its connexions with the ventricular system of the brain. *s.a.s.*, subarachnoid space; *c.m.*, cisterna magna; *c.p.*, cisterna pontilis; *c.b.*, cisterna basalis. (After Quain.)

The pia-arachnoid space is everywhere broken up into communicating compartments by delicate filamentous connexions between the two membranes enclosing it. At certain points the pia-arachnoid system has free communication with the cerebral ventricles. The chief communication is by the foramen of Magendie, a small hole in the roof of the fourth ventricle at its inferior extremity. Two small openings also exist at the sides of the fourth ventricle (foramina of Luschka). According to some authorities there are also small communicating orifices at the tips of the posterior horns of the lateral ventricles. If these communications between the pia-arachnoid and ventricular systems are blocked by plastic exudate,

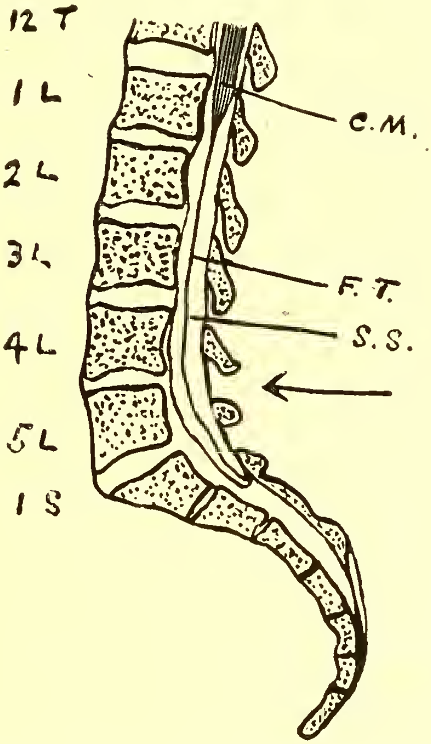

FIG. 5.—Sagittal section through the lumbar and sacral portions of the vertebral column, showing the spinal canal and its contents. *c.m.*, conus medullaris ; *f.t.*, filum terminale ; *s.s.*, subarachnoid space. The arrow shows the direction of the needle in performing a lumbar puncture between the fourth and fifth lumbar vertebræ. (After Gray.)

the cerebro-spinal fluid lying in the ventricles cannot escape, and, as the choroid plexuses continue to secrete the fluid, these cavities become gradually distended, leading to the condition termed hydrocephalus. A relative state of hydrocephalus may also occur as the result of a rapid increase in the total quantity of cerebro-spinal fluid present.

§ 2. **Physiology.**—Observation and experiment strongly suggest that the source of the cerebro-spinal fluid is the choroid plexuses. The fluid is not a transudate but a true secretion. The choroid plexuses possess a high degree of selective power in the matter of the constituent elements of the fluid which they elaborate from the blood. It has been demonstrated that they are impervious to toxic substances which have been injected into the blood-stream. This fact explains the inefficacy of such drugs as salvarsan and its allies when they are used by intravenous injection in cases of syphilitic infection of the central nervous system. This impermeability to toxic substances is evidently protective to the nerve structures and forms one of the chief functions of the cerebro-spinal fluid. Another function of the fluid is the 'water-bed' action which it exercises in preserving the brain and spinal cord from mechanical shocks. The secretion of cerebro-spinal fluid has been shown by Frazier to be diminished in animals by the administration of thyroid extract. The suggestion has been made that the exhibition of this drug may therefore be of service in the condition of hydrocephalus complicating meningitis.

§ 3. **Characters of the Cerebro-spinal Fluid in Health.**—Normal cerebro-spinal fluid is clear and limpid, quite colourless, and yields no sediment on standing. The total amount of the fluid present in the pia-arachnoid and ventricular system of a healthy adult is estimated at 60 to 80 c.c. Of this total amount some 10–15 c.c. can usually be drawn off by lumbar puncture before the flow becomes very slow. The pressure exerted by the fluid varies between 60 and 120 mm. of water; the posture of the patient affects the pressure considerably: it is about twice as much in the sitting as in the recumbent position. The normal rate of flow from a lumbar puncture needle inserted in health is about one drop in every four seconds. The fluid has a sp. gr. of 1003–1008. It is faintly alkaline in reaction. It contains a small amount of serum-albumin, the extreme limit being 0·06 per cent on actual measurement. Serum-globulin is present in a trace only. The fluid reduces Fehling's solution. A very few cells are present, the average number being 3–7 per c.mm.; the extreme limit is regarded as 10 per c.mm. These cells are almost entirely small lymphocytes; but an occasional polymorphous or endothelial cell is not to be regarded as being necessarily pathological. The fluid is, of course, sterile on cultivation.

§ 4. **Characters of the Cerebro-spinal Fluid in Meningococcus Meningitis.**

(i) *The presssure, and the amount, of the fluid.* These are both increased. Sladen found the average pressure in 75 cases observed by him to be 327 mm.

of water. This observer's highest figure was 650 mm., and his lowest figure was 160 mm. (quoted by Sophian). The amount of fluid which flows away before the normal pressure is re-established depends upon the pressure and the consistency of the fluid ; it averages about 30 c.c.

(ii) *The naked-eye appearances of the fluid.* Various grades of turbidity are met with, from very slight opalescence to a highly purulent exudate. The degree of turbidity varies with the stage of the disease at which the lumbar puncture is undertaken. In the invasion stage the fluid may be almost clear ; in the acute meningitic stage the fluid shows marked turbidity ; later, again, as the inflammatory phase passes, the fluid becomes clearer. Flakes of unorganized protein material may be present even when there is no general turbidity. The presence of blood probably always means that a vessel has been punctured by the needle : the source of the blood is generally the venous plexus at the anterior aspect of the vertebral canal. Some degree of clotting often takes place when the fluid is allowed to stand, filaments of fibrin appearing at the bottom of the tube.

(iii) *Chemistry of the fluid.* The albumin is increased in amount : instead of the faint opalescence which appears on boiling and adding dilute acetic acid to the normal fluid, a definite coagulum is produced, and an opaque ring appears when the fluid is poured gently on to the surface of strong cold nitric acid. A quantitative estimation of the albumin shows that it may be present to the extent of 0·2 or 0·3 per cent. The globulin is also increased, as demonstrated by adding one part of the fluid to five parts of a 10 per cent solution of butyric acid in normal saline, boiling, adding one part of normal caustic soda, and boiling again: a heavy white coagulum is obtained (Noguchi's test). Or the globulin may be demonstrated by allowing the cerebro-spinal fluid to drop slowly into a large beaker of distilled water: a definite trail of opalescence is seen to follow the drop as it passes through the medium. The amount of both of these substances will vary with the stage of the disease.

The reduction of Fehling's solution is said by some observers to be lost in the cerebro-spinal fluid of acute meningitis. French authors, in particular, regard this test as important. English and American authors discount the test very largely. In the writer's experience it is of no value because it is so inconstant.

(iv) *Cytology of the fluid.* The cytological picture of the cerebro-spinal fluid as seen in health changes with the presence of meningococcus meningitis. In the early or invasion stage of the disease there is a quantitative increase in the lymphocytic content, a fact which often escapes observation if the lumbar puncture be delayed. With the arrival of the acute meningitic inflammation the chief cell present is the polymorphonuclear, usually in large numbers. At the stage, therefore, at which most lumbar punctures are undertaken, the cell-content is chiefly polymorphous (70 %–80 %), following the law of Widal and Ravant as originally formulated in respect of pleuritic effusions: in effusions due to pyogenic micro-organisms the cell-content is largely polymorphous; in effusions due to B. tuberculosis the cell-content is largely lymphocytic. Later, when the stage of chronic hydrocephalus ensues, the lymphocyte again becomes the dominant cell, and in a much greater number than in healthy fluid. These transitions can usually be recognized if lumbar puncture be performed both very early, in the stage of full evolution, and in the decline of the disease. Most observers, however, describe cases of undoubted meningococcus meningitis in which the cell-content is chiefly lymphocytic throughout. In the post-basic type of the disease the cells are most often lymphocytes for the greater part, and the same may be said of cases which are in a chronic stage whilst under investigation, whether the chief seat of the effusion be at the region of the bulb or elsewhere.

(v) *Bacteriology of the fluid.* Films made direct from the cerebro-spinal fluid or, better still, from the centrifugalized deposit, show intra- and extra-cellular meningococci in the great majority of cases at some time or other in their course. If a careful search be made and no cocci are discovered, it must not be assumed that none are present until the device of incubating the fluid as a whole is undertaken, and until cultures made upon suitable media are found to be sterile (see Chap. III, § 3). The number of cocci seen, and their disposition with regard to the cells of the exudate, are matters of great variability. These things depend in the main upon (*a*) the stage

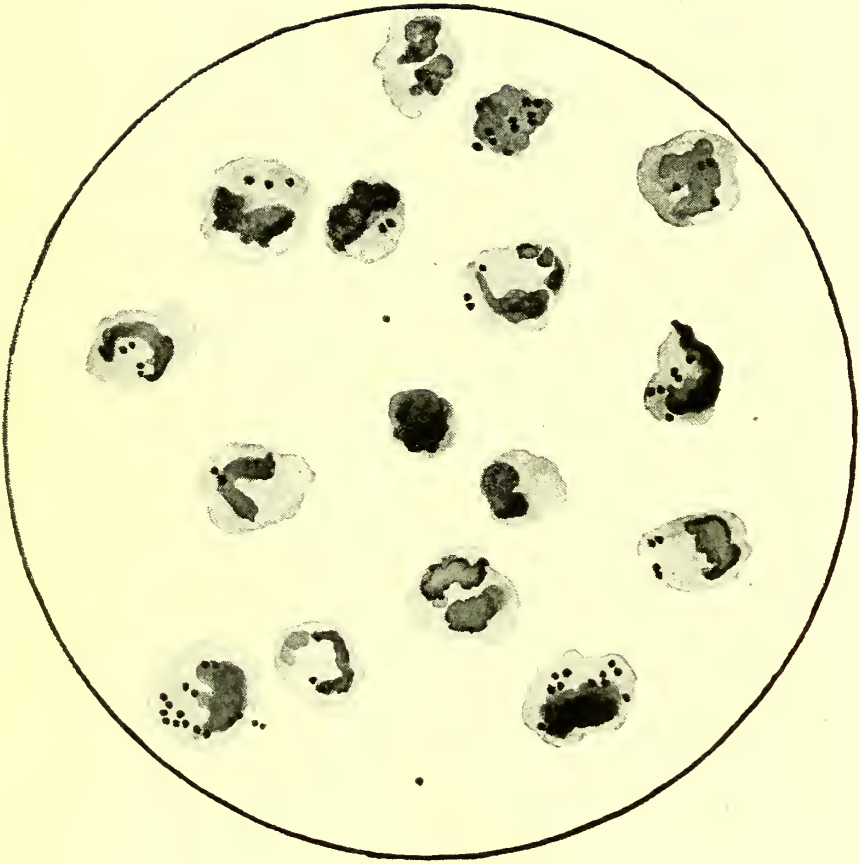

Plate I.—Reproduction of a field of the microscope (magnification 1,000) from a preparation of cerebro-spinal fluid stained by carbolthionin. The meningococci are chiefly intracellular, and are more abundant than is usually seen in such specimens. (From a preparation by Mr. E. G. Murray from a case under the care of Dr. Foord Caiger. Lumbar puncture on the sixth day of the disease. The case was of the super-acute type, and death took place on the seventh day.)

To face page 50.

of the disease, (*b*) the intensity of the infection, and (*c*) the influence of specific (serum) treatment.

(a) *The stage of the disease.* Observers differ considerably in their statements as to the bacterial content of the cerebro-spinal fluid during the first day or two of the disease. Netter and Debré say that meningococci are abundant in the fluid during the first twenty-four hours, that is, at a time when the fluid is still almost clear and the cell-content, especially in respect of polymorphous cells, is low. Sophian, on the other hand, says that at this stage of the disease the cerebro-spinal fluid is usually devoid of meningococci. Heiman appears to accept Netter's statement as being most probably correct. Most observers agree that, if cocci are present at all in the early stage of the disease, they are chiefly or entirely extracellular. As the course of the disease develops, the cocci become more constantly present, but, with the appearance of the polymorphous cells, they are chiefly or entirely intracellular. As the disease subsides, the cocci disappear, those of extracellular disposition being the first to go, then those that are intracellular. This change is concurrent with the change from a cell-exudate that is largely polymorphous back to one that is largely lymphocytic. After the first ten to fourteen days of the disease meningococci are usually absent from the fluid.

(b) *The intensity of the infection.* The more intense the infection, the more constantly is the meningococcus found in the cerebro-spinal fluid. This statement would seem to apply equally well to those cases in which there is septicæmia without meningitis as to those in which meningitis is actually present. For in the cases in which the course of the disease is too rapid to admit of meningitic changes—the patient dying with the severity of his toxic condition—the coccus still finds its way to the cerebro-spinal fluid. In other words, inflammatory changes in the membranes are later events than the appearance of the micro-organism in the pia-arachnoid space—a statement of more general application than in this particular infection.[1] *It is the cytology and the chemistry of the fluid, rather than its bacterial content, which determine the question whether or no meningitis is present.* In mild cases of cerebro-spinal fever a few intracellular cocci are found, or none at all. In abortive cases there are none. In post-basic (chronic) cases meningococci may be difficult of discovery microscopically in the exudate and still more difficult of growth in the incubator. If fluid be taken directly from the lateral ventricles in this type of the disease, the isolation of the coccus may sometimes be demonstrated when this is not possible in the case of the lumbar puncture fluid.

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[1] The mere presence of the causative micro-organism in the cerebro-spinal fluid is no proof of meningitis. Lumbar puncture performed in typhoid fever not infrequently shows the presence of *B. typhosus* in the fluid without evidences of inflammatory changes in the membranes.

(c) The use of anti-meningococcus serum brings about a rapid disappearance of cocci in most cases, especially if it be given early. According to Heiman the extracellular cocci are often already absent after the first dose, and the coccus is rarely found at all after the third dose.

§ 5. **Erratic Findings.**—It must not be assumed that the characters of the cerebro-spinal fluid, as here described in relation to the different stages of the disease, are by any means regularly observed. The fact is exactly the reverse: all sorts of variations occur, and these variations have no necessary counterpart in the clinical condition of the patient. The observer is certain to be found sooner or later completely in error if he is tempted to predict from the clinical facts, or from the course of the disease, what will be the features of the fluid at any particular lumbar puncture. Equally certain is it that he will sooner or later be found in error if he is tempted to base a prognosis upon the characters of the fluid alone (see Chap. XII, § 6). Heiman suggests that this erratic behaviour of the fluid is due to a sudden flushing of the pia-arachnoid system by inflammatory exudate from the ventricles. The moral is that it must never be assumed that the whole exudate is absorbed until definite proof of such a desideratum is forthcoming by repeated negative lumbar punctures.

§ 6. **Changes in the Cerebro-spinal Fluid in Other Forms of Meningitis.**—For purposes of comparison, reference may here be made to the condition of the cerebro-spinal fluid in infections of the meninges other than by the meningococcus. In *pyogenic infections* (streptococcus, staphylococcus, pneumococcus, gonococcus, &c.) the chemical and cytological changes do not differ from those seen in cerebro-spinal fever: albumin and globulin are increased in amount, and there is a rich cell-content, chiefly polymorphonuclear in kind. Differential diagnosis turns upon the bacteriological findings—the demonstration of the causative micro-organism in films and especially its isolation by culture. In *tuberculous infection,* although the protein is increased in amount, the increase is usually much less than in pyogenic infections. The cytological changes follow the law already referred to: the cell-content is chiefly lymphocytic (§ 4, iv). The demonstration of the tubercle bacillus is often difficult; but if the fibrin filaments which are so commonly present in the centrifugalized deposit are dealt with, the bacillus is found in a large number of cases.

§ 7. **Changes in the Cerebro-spinal Fluid in General Infections without Meningitis.**—It is necessary to touch upon this subject also, although it is one which is fraught with much difficulty. Accurate knowledge of the extent to which the cerebro-spinal fluid is altered in respect of its physical, chemical, and cytological characters, in the course of infections other than those producing meningitis, is still lacking. The reason is that investigation of the fluid by lumbar puncture in these conditions is a matter of quite recent experience, and is still limited in extent. Until lately it has been assumed that the fluid is either normal or that it presents the features already described in meningitis; whereas it is becoming apparent that changes occur in a large number of cases of bacterial infection as the result, no doubt, of toxic action exerted by the infecting agent. Briefly, these changes may be said to include an increase in the amount of the fluid, leading to a rise in intraspinal pressure, a slight increase in the protein content, and a moderate lymphocytosis. This condition of the cerebro-spinal fluid is the correlative of the clinical state termed *meningism* (see Chap. IX, § 2). During an epidemic of cerebro-spinal fever lumbar puncture is performed upon a relatively larger number of cases of infection due to microorganisms other than the meningococcus in order to establish a differential diagnosis than at times when cerebro-spinal fever is not rife. Moreover, the clinician's attention is more frequently drawn to the meningeal symptoms present in infective diseases generally at times of cerebro-spinal fever epidemics than at other times. This may be the explanation of the statements which are sometimes made, and which seem, but for this explanation, very difficult of interpretation, to the effect that during an epidemic of cerebro-spinal fever meningeal symptoms are more common in such a disease as typhoid fever than when cerebro-spinal fever is not epidemic[1] (Widal,

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[1] From private communications sent by Dr. Foord Caiger and Dr. Goodall, the writer gathers that the experience of neither of these observers lends any support to the view that meningitic symptoms are actually more frequent in

Curschmann, and others). It is obvious that a patient suffering from typhoid fever either is, or is not, suffering from a mixed infection by the meningococcus also. But in the cases quoted by these authorities the meningococcus is not found in the cerebro-spinal fluid. And when the fluid is examined in other details, the changes are those just described as occurring in highly toxic states without meningitis.

typhoid fever, &c., in England during an epidemic of cerebro-spinal fever than at other times. Dr. Goodall's explanation of the statement above referred to is identical with the one which is here suggested. Dr. Goodall writes as follows: 'May not the idea have arisen from a more keen attention to cerebral symptoms in febrile cases, whatever their nature, during an epidemic of cerebro-spinal fever? If this disease were not prevalent, the observer would not be so much struck with meningism in all sorts of cases; for this condition is not so very uncommon, even in the absence of an epidemic of cerebro-spinal fever.'

CHAPTER V

LUMBAR PUNCTURE

§ 1. **General Remarks.**—Lumbar puncture is one of the most valuable additions made to our methods of clinical examination in recent years.[1] The diagnostic and therapeutic indications for it are increasing steadily, as our knowledge of the cerebrospinal fluid and the changes which it undergoes in disease becomes greater. In any suspected case of meningitis a lumbar puncture is as clearly indicated as is puncture of the chest in a suspected case of pleuritic effusion, or a blood-count in a suspected case of leukæmia. It is, nevertheless, strange to notice with what difficulty this useful procedure has gained a foothold, especially in England. It has needed the special stimulus of an outbreak of cerebro-spinal fever to popularize the method, and even so it is probable that the majority of practitioners are unacquainted with the technique of the operation. This lack of knowledge should be repaired as soon as possible. It is not necessary to wait for an actual case of suspected meningitis in order to become *au fait* with the technique of the process, for it may easily be learnt by practice upon the cadaver in the post-mortem room. Even in the absence of this preliminary practice a successful puncture may usually be carried out when indicated by a careful study of the explicit directions given in most modern manuals of clinical methods, or by a perusal of the following sections. Ill effects from the puncture are almost non-existent, whereas the benefits to the patient, both in regard to the investigation of the cerebro-spinal fluid which it renders possible, or to the introduction by this route of immune sera, may be incalculable. The technique of the procedure will now be described in detail and in as practical a manner as possible.

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[1] The first lumbar puncture appears to have been performed by Corning, in America, in 1885, for therapeutic purposes. Four years later, Wynter, in England, punctured the theca of a child suffering from tuberculous meningitis. The operation was studied fully by Quincke about the same time, and it is chiefly owing to this observer that lumbar puncture took its place as a routine method of clinical investigation.

§ 2. **The Question of an Anæsthetic.**—If the patient is an infant it can easily be held in the position about to be described by the nurse or assistant. In an adult free from delirium a local anæsthetic (novocaine and adrenalin injection or, less suitably, ethyl chloride spray) is indicated. In stuporous or comatose patients the question of anæsthesia does not, of course, arise. In all other types of patient than these three a general anæsthetic is advisable ; these types include children who cannot be expected to understand the necessity of offering no resistance, and adults who are delirious and cannot, therefore, avoid arching the back when the puncture is made, a movement which may make the procedure very difficult. Exceptionally, also, an

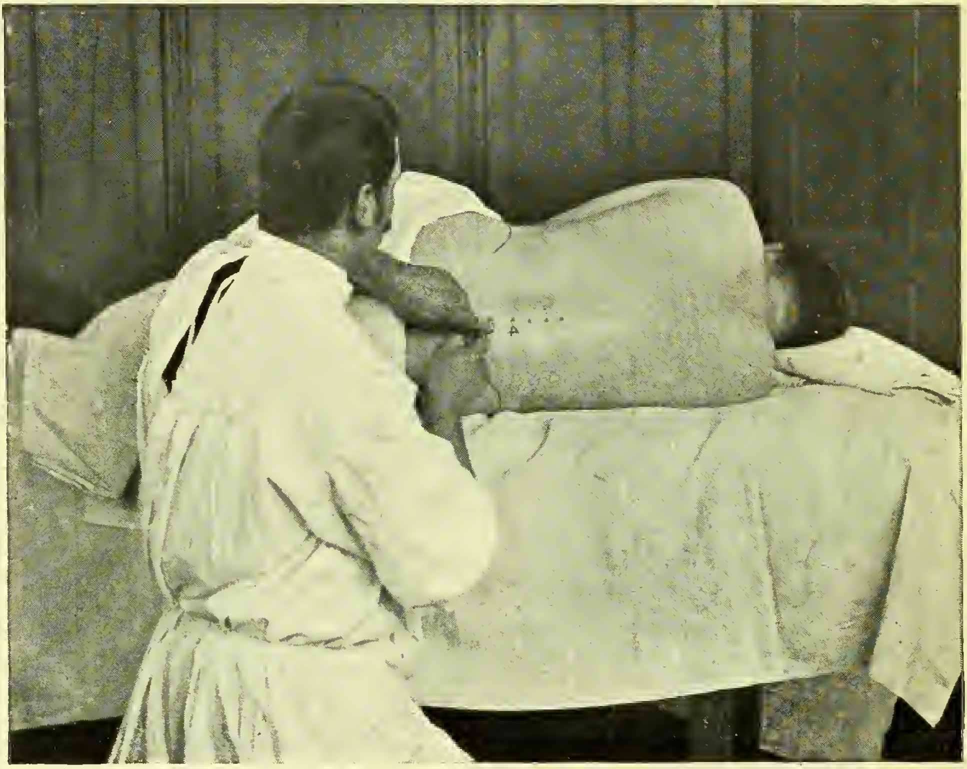

Plate II.—Illustrating the method of performing lumbar puncture.

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infant with considerable opisthotonus incidental to the disease may require a general anæsthetic in order to relax the muscles of the back. The writer does not share the views of those authors who consider the use of a general anæsthetic in very restless or delirious patients involves risk. On the contrary, he considers that in such patients the risk from the shock of the puncture (and serum administration if this be also undertaken) without an anæsthetic is greater than the risk from the anæsthetic itself.

§ 3. **Choice of Apparatus.**—Special apparatus are unnecessary. A long stout needle with a syringe may be used. But nothing is quite so useful as a ‘ Barker's needle ’, which is strongly made and is fitted with a stylet the point of which is bevelled off flush with the point of the needle, whilst the other end of the stylet terminates in a broad expansion to fit against the palm of the hand (Fig. 6). Owing to the stout make of this needle its point is not drawn out very fine; in adults a preliminary rapid piercing of the outer layer of the skin by the point of a sharp scalpel is therefore helpful. The needles—it is advisable to have a duplicate one handy—are being sterilized by boiling whilst the patient is being prepared.

§ 4. **Position and Preparation of the Patient.**—The puncture should be made with the patient in the recumbent position; even in adults who are not acutely ill no exception should be made to this rule. If the operator is right-handed the patient lies most conveniently on his right side and close to the edge of the bed. *A good light upon the back, without shadow from the* *operator's hand, is imperative.* The shoulder is on the bed, and not on a pillow, so that the spine lies straight in its long axis. The knees are drawn well up to the abdomen, and the head and shoulders are bent forward: the trunk is thus arched with its convexity backwards (Plate II). This position is best secured in an infant by one arm of the nurse or assistant being placed round the neck and the other arm under the knees. By clasping hands, the infant's body can be brought into the desired posture.

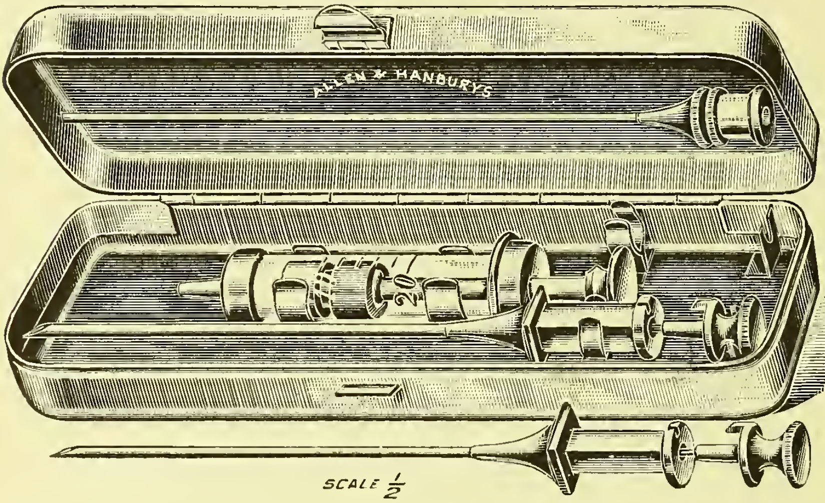

FIG. 6.—Barker's needles. The syringe is not used for the lumbar puncture, but for the administration of serum if the injection method is employed.

Sterilized, or, failing this, clean towels are placed around the site of puncture—the region of the sacrum and lumbar spine. The skin in this situation is now rubbed thoroughly with acetone or alcohol, or is swabbed with tincture of iodine.

§ 5. **Surface Marking for the Puncture.**—Anatomical considerations make the space between the fourth and fifth lumbar vertebræ the most convenient one for the puncture. This point is well below the conus medullaris; the vertebral interspace is here at its largest; the dorsal spine of the fourth lumbar vertebra is disposed at right angles to its body. (See Fig. 5.) But the interspace above or below the fourth may be utilized with almost equal advantage. This space is cut by a straight line joining the summits of the two iliac crests. The most useful landmark is the spine of the fourth lumbar vertebra, which is the one lying nearest to this intercristal line. The puncture is made between this spine and the one lying next below it, which is felt at a distance of a half to one and a half inches, according to the patient's age. *It is essential to success to outline the two spines beyond any doubt* (Fig. 7).

§ 6. **Making the Puncture.**—The puncture is made in the middle line and directly forwards. The needle is grasped firmly, its base lying against the palm of the hand. The skin is supported by firm pressure with the thumb of the left hand. In adults it is sometimes found better to direct the needle slightly upwards. If obstruction be encountered this is probably by bone: the tubercle projecting downwards from the under surface of the dorsal spine above, or one of the laminæ surrounding the space aimed at. The needle should be withdrawn a very little way and redirected slightly, with a view to correcting any fault which may be suggested by a revision of the surface markings. The needle is often felt, in a successful puncture, to enter the ligamentum subflavum and the dura mater quite distinctly. To reach the canal the needle is found to be inserted a distance varying from one to three inches according to the size of the patient.

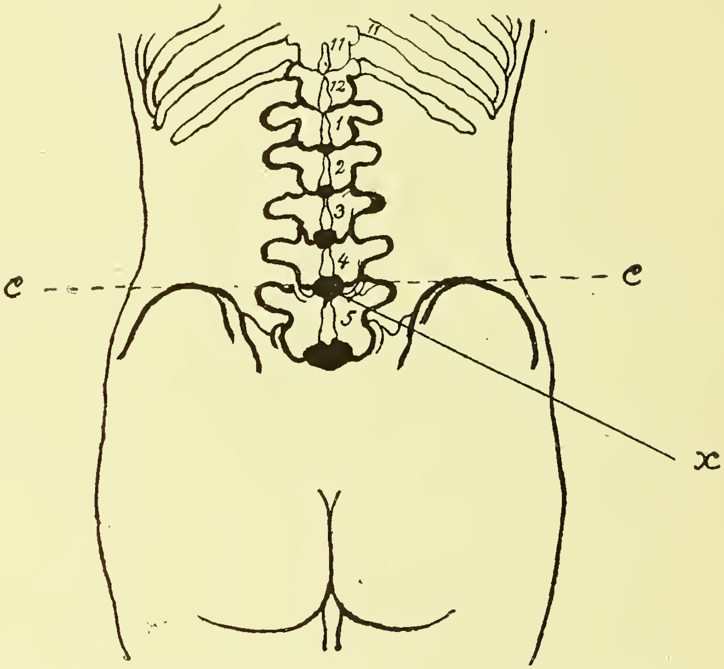

Fig. 7.—Diagram illustrating the region concerned in the performance of lumbar puncture. *c c*, the intercristal line; *x*, the space between the fourth and fifth lumbar vertebræ, the space of election. (After Heiman and Feldstein.)

As soon as it is judged from the 'feel' of the needle that it has entered the subarachnoid space, it is advisable to test its position before pushing it further forward. In this way the operator avoids piercing the venous plexus which lies at the opposite side of the canal, and which forms the common source of the blood that occasionally flows and obscures the result of the puncture. If such an accident happens it will often be found that slight traction on the needle in the direction of its handle will result in a flow of fluid free from blood ; in this case the fluid should now be collected in a separate vessel.

If a 'dry' puncture results, it is because the needle has not entered the canal at all, remaining epidural or missing the interspace altogether and lying at the side of the vertebra, or has struck a nerve-root which blocks its orifice, or because the inflammatory exudate is too thick to flow through it. The first possibility is the most probable, especially with an operator who is not very experienced ; the last is very uncommon.

§ 7. **Collection of the Fluid.** Assuming Barker's type of needle to be used, the first three or four c.c. of fluid are allowed to run into an ordinary clean test-tube and are utilized afterwards for chemical tests which will go far to establish the diagnosis by the bedside (see Chap. IV, § 4). A sterile bottle or test-tube is then placed to receive the rest of the fluid, care being taken to avoid contaminations from the air, hands, &c. The bottle or tube is carefully sealed and is sent forthwith to the pathologist. If it cannot be dealt with in the laboratory within two hours some arrangement must be made for keeping the tubes warm, as by wrapping them in cotton-wool and placing them in proximity to a hot-water bottle.

The *amount* of fluid drawn off will depend upon its nature and upon the pressure under which it exists. In general it may be said that *the fluid may be allowed* *to run away until the rate of flow is reduced to one drop to each three or four seconds.* The needle is now withdrawn by a quick movement, the skin being supported by firm pressure with the thumb of the left hand. The minute hole is sealed by a small piece of gauze soaked in collodion.

CHAPTER VI

CLINICAL TYPES

Cerebro-spinal fever is protean in its features and especially in its modes of onset. The experience even of those observers who have seen much of the disease is being constantly enriched by novel manifestations of the infection. To have studied a number of cases during a particular epidemic gives a very valuable insight into the disease, but, as the symptom-complex changes from epidemic to epidemic, familiarity with one set of cases by no means suffices to ensure facility in the diagnosis of another set. The careful observer of a large number of sporadic cases is quite as likely to be cognizant of the different possibilities of the causal micro-organism as is the student of an epidemic, because the material dealt with by the former is apt to be even more varied.

Out of the large number of different manifestations that occur, certain cases repeat themselves with sufficient constancy to constitute clinical 'types', capable of description and of recognition. After dealing with these types some reference will be made to aberrant forms of the disease.

§ 1. **The Ordinary or Acute Type.**—The *incubation period* is difficult to estimate with accuracy; there are reasons for considering it to be four or five days, but the number of cases in which it can be gauged are few. The illness begins with the usual symptoms of an acute specific fever, and for the first day or two, or for longer than this if the possibility of the disease under consideration is not borne in mind so as to lead to a special examination, there may be nothing to distinguish the illness from one or other of several acute febrile infections.

The *onset* is usually sudden, with fever, headache, general malaise, and vomiting. The *temperature* usually rises rapidly and attains a fairly high degree on the first day (102°–104°).

The *headache* is apt to be very intense, is often referred to the occiput, and shows little or no response to the customary palliative drugs given to relieve it.

There is frequently a *rigor* in the adult, or a *convulsion* in the infant or child. *Vomiting* is more often met with in children than in infants, and is quite common in young adults.

In addition to the three cardinal symptoms at the onset, headache, fever, and vomiting, the following are quite common, but are not nearly so constant: *delirium, pains in the neck and limbs,* and some degree of *catarrh* either of the nose, naso-pharynx, conjunctiva, or ear. In some cases there is considerable *bronchial catarrh* and in others definite *enteritis*. In addition to the pains referred to the limbs there may be pain and *swelling of the joints.*

After some two to four days of these initial symptoms evidence of meningeal irritation begins to show itself in more or fewer of the following developments. The *vomiting* is repeated despite the fact that the invasion symptoms are past. The *pulse* is irregular in rhythm, and in older children and in adults it is often relatively infrequent when compared with the height of the temperature. The *respirations* are irregular. The *vasomotor system* is unstable, leading to periodic flushing of the face and to the presence of *tâches cérébrales*. The patient lies on his side with legs drawn up and prefers the shelter of the bedclothes. The *pupils* are dilated and the light reflex is sluggish. There is *photophobia* with intolerance of noise and of all kinds of interference. Examination of the *neck* reveals a *stiffness of the muscles*, which cannot be overcome without pain. The *hamstrings* are found to be taut, so that the knees cannot readily be extended if the hips are flexed (Kernig's sign). The *abdomen* is retracted and the superficial reflexes are abolished. The *mental state* is one of restlessness and mild delirium with troublesome insomnia. The *headache* may become quite intolerable and may require morphia for its reduction. In a considerable number of the cases a *rash* appears during the first week—either a number of large rose-spots about the trunk and limbs, or a macular eruption like that of measles, or a few small petechiæ scattered over the trunk, neck, and extremities. *Herpes* is common, and is generally situated at the usual places—the angle of the mouth, the chin, and the nose. There is a leucocytosis of considerable degree (20,000–40,000).

Towards the end of the first week the mental state changes to a condition which may perhaps best be described as one of *resistant stupor*: the patient can be roused by an effort at examination or by a change of position; but either proceeding is resented and he quickly resumes his huddled posture. The headache is less constantly severe, but shows sudden and marked exacerbations, often nocturnal, with complete insomnia. The neck rigidity increases and the *head is retracted.* The back also becomes stiff. Flesh is lost rapidly. Polyuria is common, with polydipsia. The temperature generally remains fairly high, and, although this is by no means invariable, the fever approximates to the continued type.

Assuming the course of the disease is not interrupted by lumbar puncture or by specific therapy, the condition of the patient remains much the same during the second, and perhaps during the third, week of the illness. But the wasting continues. The temperature often becomes intermittent in type. One of three modes of termination will be followed.

(a) *Recovery.* This is gradual when it occurs, and is often interrupted by sudden *recrudescences*, throwing the patient back into a state which leads to renewed anxiety. Even when a marked remission has occurred in the main symptoms the patient is by no means safe from these ‘ crises ’, which form a striking feature of the disease. They may be due to an extension of the infective process into some further area of the pia-arachnoid system, or to mechanical events connected with the condition of acute hydrocephalus that exists, or to both of these things. The temperature chart is often interrupted in its defervescence by sudden rises, with or without a corresponding recrudescence of the meningitic symptoms. Ultimately the fever completely subsides, the patient ceases losing flesh, the headache and stupor pass off, and the rigidities slowly disappear. The pulse-rate remains high for some time in a good number of cases, and some authors regard this as a sign that the patient is not yet free from the possibility of relapse, and therefore as an indication for caution in treatment. The actual stage of *convalescence,* once it is established, is rarely interrupted. If the temperature and pulse-rate have remained normal for fourteen days, the risk of relapse may be considered to be passed. It may be some weeks, however, before the patient is free from stiffness.

(b) *Death.* The ordinary type of the disease is not often fatal during the first two weeks. When it is, the stupor passes into true coma, the pulse and respiration rise in frequency, and the temperature often shows a sudden ante-mortem rise.

(c) *Becoming chronic.* More often, if the ordinary type terminates fatally, it is by passing into a subacute or chronic stage. If the 'crises' already referred to continue, or if, despite the fall of temperature, there is no corresponding improvement in the general condition, a condition of progressive emaciation supervenes, with a tendency to chronic hydrocephalus. The wasting is sometimes extreme, so that bedsores are unavoidable. The rigidity becomes marked, and approaches, even in adults, that degree termed cervical opisthotonus in infants. Feeding becomes difficult, and this adds to the wasting due to trophic disturbances. The sphincters usually relax, leading to incontinence. Optic neuritis develops. The patient may continue in this unsatisfactory state for several weeks, or even months, and yet may eventually recover, and without any residual defects. More often, however, he gradually succumbs to the disease, or, if he eventually survives its ravages, it is to be left with mental defect, deafness, blindness, or hemi- or diplegia.

Opinions differ as to the frequency of true *relapses* in cerebro-spinal fever. This is probably due to the fact that what some authorities term relapses others consider to be recrudescences merely. It is certain that the latter are very common; indeed, they are a characteristic feature of the disease. Reference has just been made to them (§ 1 (*a*)). The reader is also referred to Chap. VII, § 6, and to Chap. XIII, § 10.

§ 2. **The Superacute Type.**—This form of the disease is common at the height of an epidemic. The invasion symptoms are abrupt, and the patient is from the first very ill. Delirium is marked, with most tiresome insomnia, and the headache may drive the patient to a state of acute mania. The temperature is usually very high (104°–106°), and intermits. Skin eruptions are more constantly present than in the ordinary type, but are by no means necessarily petechial in character. Discharges are apt to occur from the nose and conjunctival sac. The tongue is dry and tremulous. The meningococcus can generally be grown from the blood by culture, and may even be demonstrated in cover-slip preparations made from the blood direct. The leucocytosis is high (30,000–40,000). After three or four days the active mental state changes to stupor; if the cerebral pressure is not now relieved by lumbar puncture this stupor passes into coma. Even if the pressure is relieved by this procedure there is a great tendency for the patient to slip back into a comatose state; then, with pulse, respirations, and temperature all rising, with insensitive pupils and absence of corneal reflex, the surface of the body becomes livid, the lungs congested, and death occurs.

§ 3. **The Fulminating or Malignant Type.**—This form is prone to occur during the evolution of an epidemic. But it is by no means rare as a sporadic manifestation of the disease. It is more often seen in older children, adolescents, and adults than in infants and younger children. The abrupt appearance of fever, headache, and active delirium, rapidly passing into coma, the whole course of the disease may not exceed twelve hours. It may even be less: '. . . he went out to his father to the reapers. And he said unto his father, My head, my head. . . . And when he had taken him, and brought him to his mother, he sat on her knees till noon, and then died.'

It is the occurrence of these fulminating cases that accounts for much of the horror associated with the disease in the lay mind. During an epidemic it is common to read newspaper records of inquests held upon victims of this type of cerebro-spinal fever, death having occurred so quickly as to afford no clue to the nature of the malady in the mind of an unsuspecting practitioner. A question of foul play may be raised on account of the highly toxic condition observed by the medical attendant. In some of the cases a diagnosis of cerebral hæmorrhage is made. The more abrupt cases of polio-encephalitis may also cause difficulty in diagnosis (see Chap. IX, § 5).

In all fulminating cases of cerebro-spinal fever there is a rapid development of septicæmia. In some of them the septicæmia covers the whole of the disease, symptoms of meningitis being absent and the meninges being free from gross lesions on examination post mortem. Even more constantly than in the super-acute type is a blood culture positive, but the course of the disease is too rapid to admit of a diagnosis by this method during life. If, however, the practitioner is sufficiently alert to examine blood films, he may succeed in proving the nature of the disease, though he will not thereby save his patient.

§ 4. **Mild Types.**—These cases are said to be common during the decline of an epidemic. It is at present quite impossible to say with what frequency they occur, because it is certain that many of them are overlooked. They are often treated as cases of ‘ influenza ’, owing to the resemblance they bear to that disease. Many cases of acute fever with headache and pains in the back and limbs are regarded as ‘ influenza ’ from a diagnosis by exclusion. They are not subjected to a lumbar puncture because the condition does not seem sufficiently grave. And if they recover after an illness of a few days’ duration this is thought to be confirmatory of the diagnosis. In the presence of an epidemic of cerebro-spinal fever, however, a very close scrutiny of these cases should be made, and if there is even doubtful neck-rigidity or Kernig's sign, the cerebro-spinal fluid should be examined. Even when lumbar puncture is not at first decided upon a swab from the naso-pharynx should be investigated for the meningococcus.

During an epidemic a patient who presents the symptom-complex of headache, malaise, pains in the back and limbs, slight fever, and some stiffness of the neck, is probably suffering from a mild grade of meningococcus infection, and should be treated as such, by a lumbar puncture and the administration of serum. Subsequent measures will be determined by (*a*) the course of the disease ; (*b*) the result of the examination of the cerebro-spinal fluid ; and (*c*) the result of the examination of the naso-pharyngeal swab.[1] The value of these cautionary measures is sometimes made apparent by the patient becoming rather suddenly worse after a few days, when it may be quite obvious that the nature of the disease is what was originally suspected.

These mild cases are referred to again in the chapter on diagnosis, because the consideration of them is very largely a diagnostic problem. Heiman says that this type of the disease may 'attack' a large number of individuals in a school, regiment, or village. It is obvious, however, that such a statement, though the phenomenon is likely enough, requires full bacteriological evidence to support it. Small epidemics of infection by M. catarrhalis have been described, in which many of the cases developed symptoms not unlike those of meningeal irritation; such a fact makes the fullest investigation essential in all suspected epidemics of mild cerebro-spinal fever.

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[1] An exactly analogous mode of procedure is adopted in a case suspected on clinical grounds to be diphtheria.

§ 5. **Post-basic Meningitis of Infants (Cervical Opisthotonus of Infants).**—These cases were first described (1878) by Gee and Barlow. These observers recognized that they were dealing with a specific disease which had no causal association with tuberculosis, syphilis, or rickets. At the time of these authors' observations no epidemic of this type of meningitis had been described, and the cases were thought, even by much later writers, to be met with in sporadic fashion only. Of recent years, however, it has been recognized that this clinical manifestation of meningococcus infection may occur in epidemics.

The characters of the micro-organisms present in these cases were originally thought by some workers to differ from those of the micro-organisms found in the acuter cases occurring in epidemics. This distinction has disappeared of late, and there is more or less consensus of opinion that, although the strain may vary, the causal diplococcus is essentially the same in the acute as in the chronic, and in the epidemic as in the sporadic cases.

Seeing that the clinical features, again, do not differ materially in this type of meningitis from those often seen in cases occurring in older children, and occasionally even in adults, nor from those often seen in infants at times of an epidemic, it follows from these considerations that the inclusion of cases of post-basic meningitis in a general account of cerebro-spinal fever is amply justified.

Post-basic meningitis occurs chiefly in infants between the ages of six months and two and a half years. The same type of the disease may, however, be seen in children up to the age of four or five years. The onset is usually sudden, with a convulsion in many cases, and very frequently vomiting. The temperature rises abruptly, but does not, as a rule, remain high. In most cases the fever has become slight, or is absent, by the end of the first week of the illness. Therefore in many cases the disease is afebrile by the time the patient comes under careful observation. A large number of the patients suffering from the disease are without fever when they come under observation.

The main and characteristic sign of the disease, the retraction of the head, becomes marked about the third or fourth day. It usually persists, with increasing severity, throughout the whole course of the disease. With it the back becomes arched, so that in extreme instances the occiput and the sacrum may meet. The extremities are usually in a condition resembling tetany, the stiffness being persistent rather than paroxysmal. Progressive wasting is another constant feature, and the degree of emaciation is often very considerable, and very rapid. Of the other symptoms vomiting is one of the most common, and may be very troublesome. The pulse and respirations are usually frequent, and may be irregular.

The disease in most cases quickly enters upon a chronic course. The infant lies motionless in its characteristic attitude for hours at a time, but is not usually comatose. Feeding is not as a rule difficult. The pupils are fully dilated. Blindness is present sooner or later in thirty per cent. of the cases (Langmead), the origin of the condition being central, since optic neuritis of any magnitude is quite uncommon. Blindness is rare in the cerebro-spinal meningitis of older children and of adults.

Lumbar puncture yields similar results to those found in the ordinary type of the disease, but as the condition progresses it is found that the meningococcus fails to appear in the fluid, and the polymorphonuclear cell-content changes to a lymphocytosis, indicating the chronic stage of the infection. Dry punctures are not uncommon, indicating the probable closure of the foramen of Magendie by the plastic exudate at the region of the bulb and fourth ventricle. Fluid removed from the ventricles during life, or the examination of fluid found in the ventricles post mortem at this stage, often reveals the meningococcus, showing that the disease is still, in its chronic phase, to be regarded as a persisting infection. Indeed, the post-basic meningitis of infants is probably to be considered as a meningococcus infection of the pia-arachnoid system with a special tendency to involve the cerebral ventricles by ependymitis. The peculiar symptoms and course of the disease are thus explained.

Owing to the early development of hydrocephalus in this type of the disease (see Chap. VIII, § 1), and the elastic nature of the infant's skull, the head enlarges in all directions, with bulging of the fontanelles and opening of the sutures between the bones. The shape of the skull thus approximates to that of congenital hydrocephalus. The eyes are turned downwards, and the sclerotics above the cornea are exposed by retraction of the upper lid. If this condition of acquired hydrocephalus has lasted for some weeks there may be enlargement of the superficial veins about the nose and orbits and running over the temporal regions to the vertex. Macewen's sign (see Chap. VIII, § 3) is not obtained because the fontanelles are still patent.

The mortality in this type of the disease is very high, probably over eighty per cent. Some of the cases linger for many weeks, and a few very gradually recover, with, all too often, a residual blindness and perhaps deafness also. But the majority succumb to the intracranial pressure effects produced by the distended ventricles, in from four to six weeks from the onset of the disease.

§ 6. **Aberrant Forms.**—In addition to the five clinical types of the disease above described, there are some other varieties, but they scarcely deserve individual description.

(i) *Abortive cases.* It occasionally happens that a patient whose illness began with abrupt onset, severe general symptoms, and early and definite meningeal involvement, becomes rather suddenly much better in every respect about the third or fourth day, and his convalescence begins straight away. Such an event is sometimes seen with almost, if not all, acute specific infections ; and there is no more to say.

(ii) *Intermitting cases.* A name given somewhat unnecessarily to the cases in which the fever is of the intermittent type. The intermission may be quotidian or it may be tertian. In the latter cases, strangely enough, the administration of quinine may bring about a defervescence ; yet the existence of malaria can be certainly excluded. There is quite commonly a tendency for the type of fever to become intermittent towards the end of the infection, as will be noticed in more than one of the charts reproduced in Chap. VII.

(iii) *Cases of cerebro-spinal fever simulating other diseases.* It is for the most part in the mode of onset and in the symptoms of the period of invasion that the simulation exists. The likeness is probably due to actual lesions present in the organs which contribute the equivocal symptoms. These lesions can now and again be demonstrated to be the result of an associated meningococcus infection ; at other times they can be proved to be due to a mixed infection.

Some authors speak of the ‘ typhoid variety ’ of the disease. If the abdomen is distended and the spleen is palpable, the intense headache with fever of a continued type is strongly suggestive of *typhoid fever.* E. Milligan met with such cases in the Belfast epidemic of 1907.

In children the bronchial catarrh, a certain amount of which is quite common in cerebro-spinal fever, may be very marked; a true *broncho-pneumonia* may occur. For some days such cases may be treated as though the pulmonary lesion covered the whole infection, the nerve symptoms being attributed to a toxæmia. In other children, and in some infants, the symptoms of *gastroenteritis* may form the most manifest part of the clinical picture.

The writer has seen two cases in young adults in which a diagnosis of *rheumatic fever* had been made, owing to the strong clinical resemblance to this disease. In one of these patients there were, in addition to the acute synovitis, very profuse sweats of a strongly acid odour.

CHAPTER VII

DETAILED SYMPTOMATOLOGY

In this chapter the main symptoms and signs of the disease will be considered in detail, with such references to the clinical types of cases just described as may seem appropriate. The symptoms here dealt with must be regarded as constituting, in collective fashion, a composite picture of the disease as it would be seen if a large number of cases occurring in different epidemics, and also sporadically, were fused into one. It cannot be emphasized too often that the clinical manifestations of the disease are protean, and that enormous variations occur, not only in the degree to which the several symptoms exist, but also in their existence at all in different cases.

§ 1. **Facies and Posture.**—The eyes are usually bright, with clear conjunctivæ; the face is flushed, but owing to the vaso-motor instability, which is an early sign of nerve involvement, the flushing is apt to vary from hour to hour. The patient is often noticed to choose the lateral position quite early in the course of the disease, and is uncomfortable if placed on the back. Such an observation should always lead to an examination of the muscles of the neck, which are then found to be a little stiff. The legs are often kept bent at the knees, with the hips partially flexed.

§ 2. **The Mental State.**—In the ordinary type of case the first few days are characterized by excitement and restlessness, or by actual delirium. Insomnia is often a most troublesome symptom. Towards the end of the first week periods of stupor often interrupt this mental activity, but it is not difficult to rouse the patient by efforts at examination. Exacerbations of the restlessness, with complete insomnia, and with added intensity of the headache, contribute to produce a picture which is rarely seen in any other disease. These ' mental crises ' are, however, much less serious in their significance than the state of coma to which the fulminating form of the disease reduces its victim after a few hours, or which follows upon a failure to recognize the nature of the disease until the intracranial pressure resulting from the acute hydrocephalus becomes very high.

In mild cases the mind remains clear and unaffected. In infants and little children, even when the disease is acute and severe, there is not, of course, any delirium, but only great irritability and intolerance of examination. If the disease passes into the chronic stage this state of irritability changes to one of apathy. In infants this is very striking, the patient lying for hours together motionless and silent.

§ 3. **Skin Eruptions.**—These are very variable, both in different epidemics and in different stages of the same epidemic. In quite a large number of cases there is no skin eruption present at all. The statement that, when present, skin eruptions are due to some 'secondary infection' appears to have been made without any reason to support it.

(a) *Hæmorrhagic rashes.* The small dark petechiæ, which gave the name 'spotted fever' to the disease, are often quite absent. They are more common in fulminating and in very acute cases than in those that are less severe. These spots are apt to appear much more frequently in some epidemics than in others. They are rarely very extensive in distribution, often at most a few isolated spots about the chest, abdomen, and thighs. But they are occasionally very profuse indeed, so that the whole body is covered with minute purpuric spots like flea-bites. Another variety of hæmorrhagic eruption consists of much larger areas, few in number, and usually confined to the back. Osler described an erythema about the extensor aspect of certain joints which developed into a bullous hæmorrhagic stage.

(b) *Discrete red papules.* More common, perhaps, than the purpuric spots is the appearance, during the first three or four days, of large rose spots scattered discretely over the body and (unlike the rose-spots of typhoid) involving the arms and legs as well as the trunk.

(c) *Diffuse rashes.* More equivocal rashes, macular or, less often, scarlatiniform in character, may appear later in the course of the disease. These raise difficulties in diagnosis from the acute exanthemata which they resemble, especially if the day of their appearance in relation to the first day of the disease be not taken into account. These rashes are apt to be very evanescent and they not infrequently synchronize with an exacerbation in the meningeal symptoms.

(d) *Herpes.* Herpetic eruptions are said by some observers to be even more common in this disease than in pneumonia. But it is clear from the accounts of various epidemics that the appearance of herpes is by no means constant; indeed, in some epidemics it is notoriously absent. Nor is it at all common in sporadic cases. When present the vesicles are not very extensive, but they may involve other areas than the customary one about the mouth and nose, such as the palate, the eyes, and the hands and feet.

(e) *Serum rashes.* If serum is used a rash may be expected on or about the ninth day from the first administration. This is later than (b), which it most closely resembles. It is often urticarial in character—another differential feature.

§ 4. **The Pulse.**—The *frequency* of the pulse is increased, but in older children and in adults the frequency is quite often relatively less than is proportionate to the height of the fever. In little children and in infants this relative pulse infrequency is not seen. Moreover, if the case is very severe in type, again there may be no relative infrequency. The pulse frequency is very apt to vary much from hour to hour, and from day to day, even when the minimum frequency is high. The writer regards this feature as one of considerable diagnostic importance. The general lack of correspondence between pulse frequency and height of temperature, and the variations in pulse frequency from hour to hour, are illustrated in the accompanying chart (Chart 1). For comparison, similar charts of temperature and pulse-rate in cases of pneumonia (Chart 2) and typhoid fever (Chart 3) are given. Quite apart from pulse frequency, it will be found that the *rhythm* of the pulse is very often affected, leading to irregularity. This feature, again, is in striking contrast with other acute febrile processes, especially at their

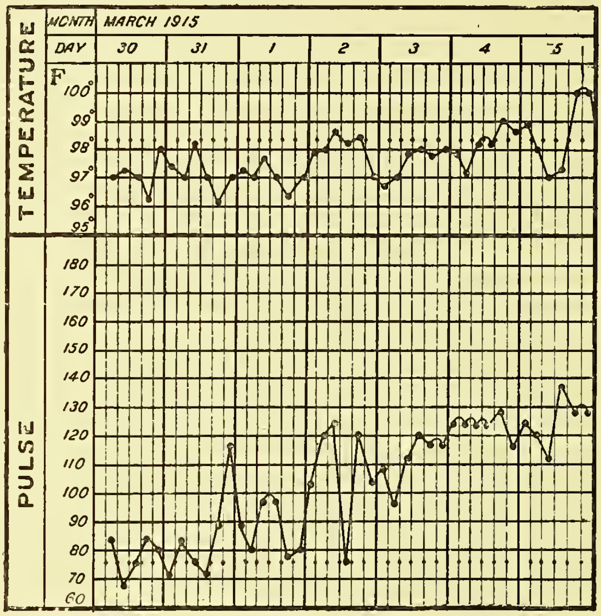

CHART 1.—Showing the pulse and temperature curves during one week in a case of cerebro-spinal fever. To illustrate the marked irregularities in pulse frequency at different times of the day and the lack of correspondence between pulse frequency and height of fever.

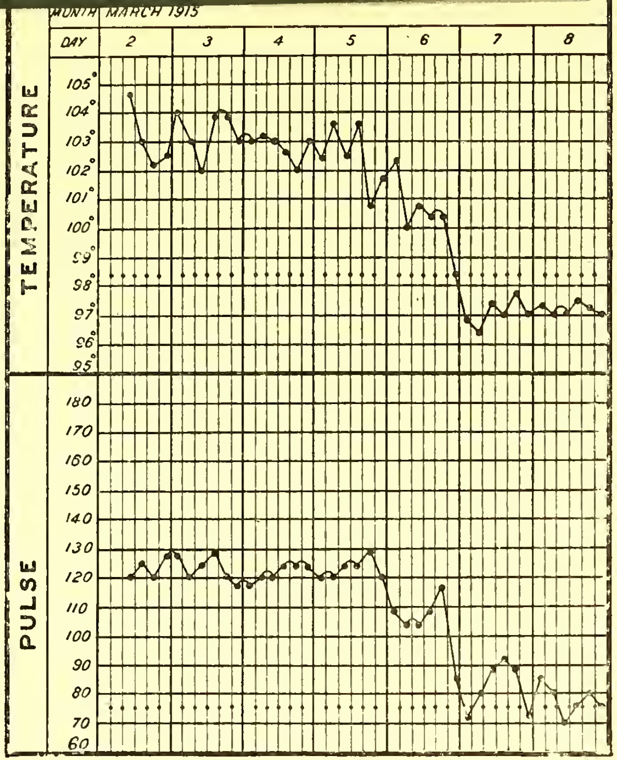

CHART 2.—Showing the pulse and temperature curves during one week in a case of pneumonia. To illustrate the relative uniformity of pulse frequency and the correspondence between pulse frequency and height of fever.

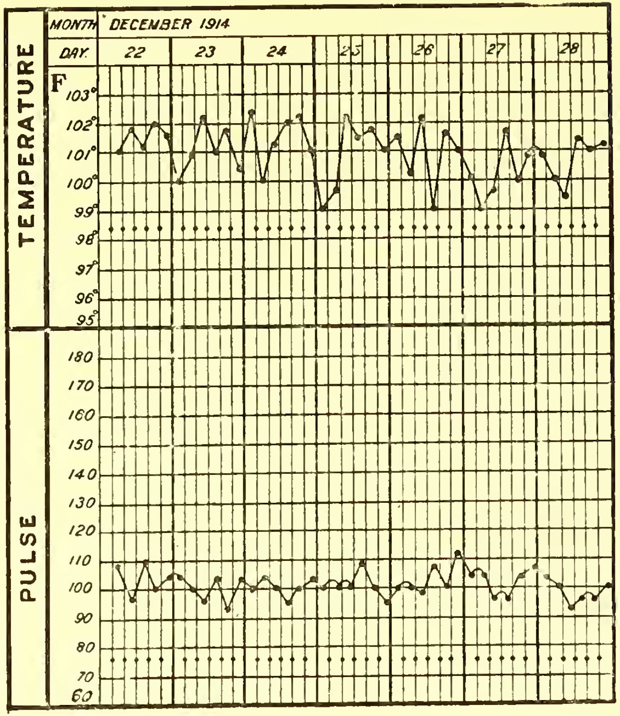

CHART 3.—Showing the pulse and temperature curves during one week in a case of typhoid fever. To illustrate the relative uniformity of pulse frequency and the correspondence between pulse frequency and height of fever.

outset, and when there is no question of any cardiac complication.

§ 5. **The Respirations** are frequent and, like the pulse, are apt to show irregularity in rhythm. The irregularity is often of the Cheyne-Stokes variety, especially in little children. But in older children and in adults a more common type of irregular breathing occurs, less periodic, and showing intervals of apnœa or deep sighs.

§ 6. **The Temperature.**—The fever of meningococcus meningitis is of no very constant type. In nearly all cases the temperature rises suddenly. The chart may show two or three days of a high quotidian intermittent fever at the outset (Chart 4), or it may show a continued fever, not unlike typhoid, from the first (Chart 5). In quite a considerable number of cases the type of fever can only be termed irregular, falling gradually to normal with the subsidence of the symptoms (Chart 6). A few cases, and these are not necessarily mild ones, are almost or quite afebrile. By the time the post-basic cases in infants come under observation they are usually afebrile.

The use both of lumbar puncture and of serum interrupts the course of the fever very frequently. Chart 5 is of interest because neither of these remedies was employed in the treatment of the patient. The effect of lumbar puncture is to lower the temperature, and there is not, as a rule, any preliminary rise. The use of serum also lowers the temperature in most cases, but an initial rise very frequently precedes this event (Charts 4 and 8). This immediate effect

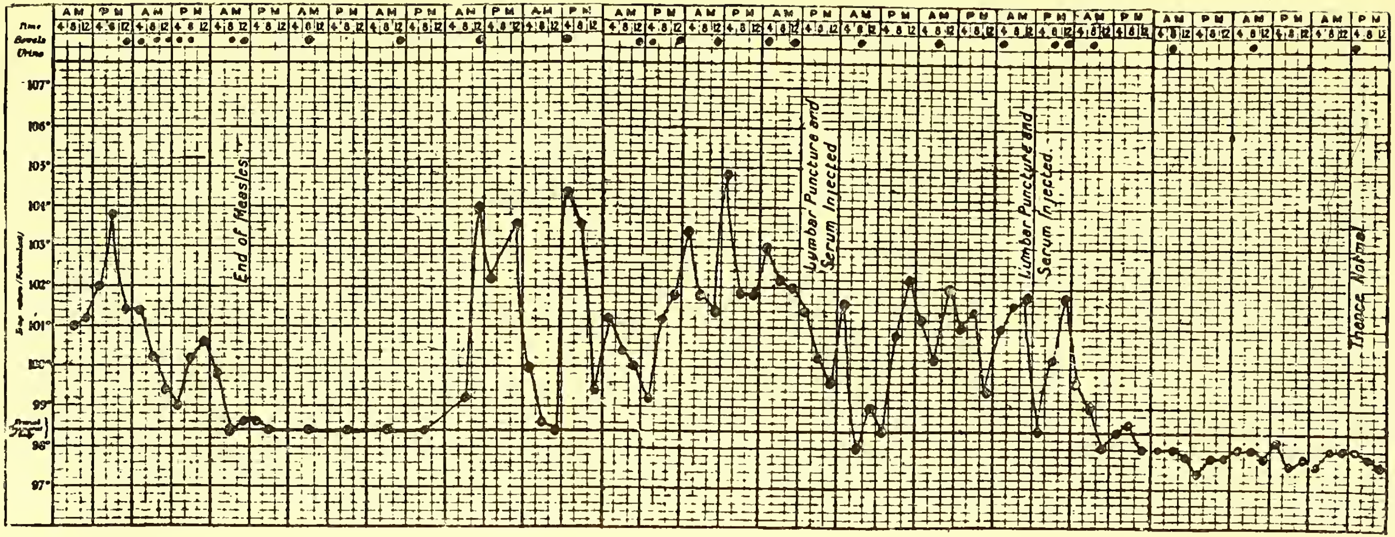

CHART 4.—Illustrating the sudden onset of an attack of cerebro-spinal fever in a schoolboy aged thirteen years, on the fourth day after defervescence from measles. The boy being still under observation, and in bed, the abrupt form of onset of the disease is clearly seen. The chart also illustrates the fall of temperature due to lumbar puncture and the use of serum on the fifth and eighth days of the disease respectively.

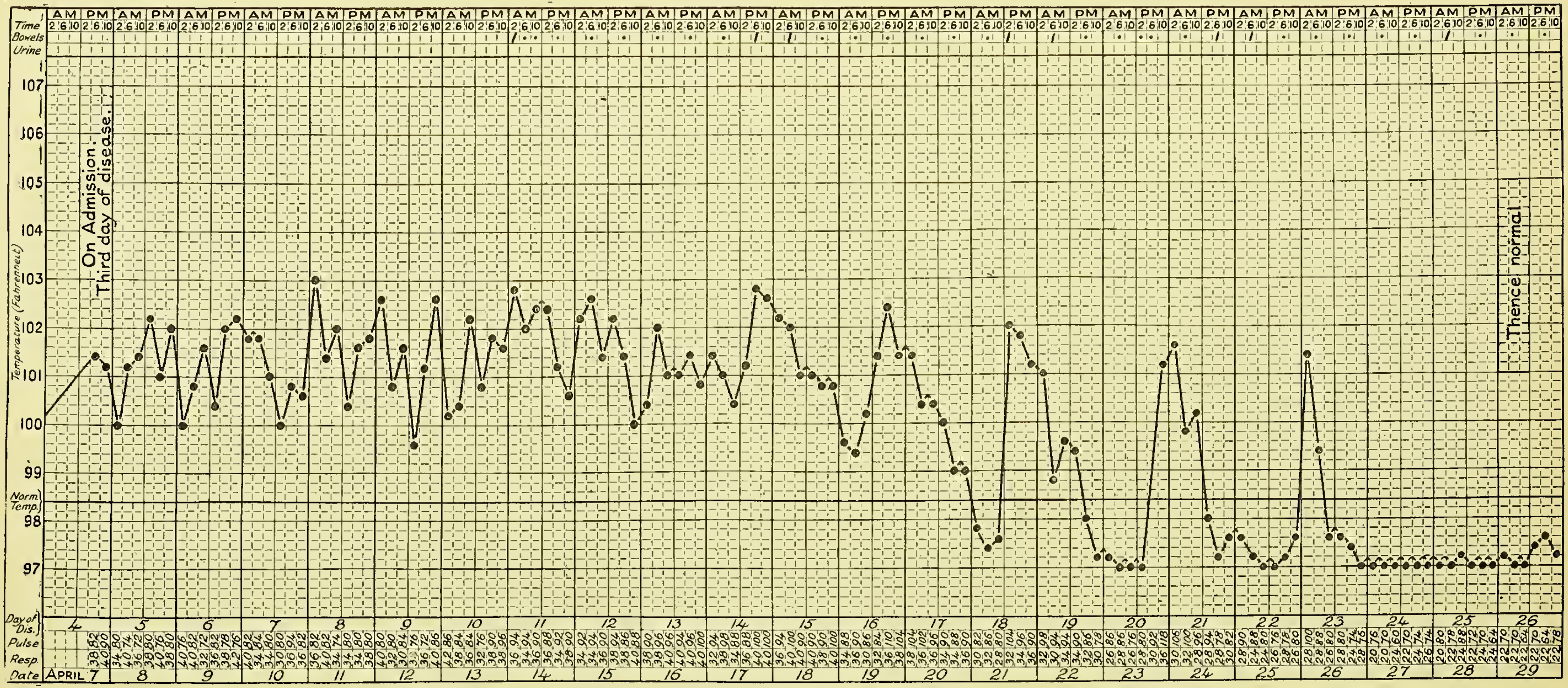

CHART. 5.—Illustrating a common type of fever in cerebro-spinal meningitis, continued fever with slight remissions for a fortnight, followed by intermitting fever for the third week. The case was not treated by lumbar puncture nor by serum administration, but only by urotropin; the temperature chart is therefore uninterrupted, and probably represents a natural course. (From the case of a soldier, aged thirty-nine years, under the care of Dr. Prior, at the Hornsey Fever Hospital.)

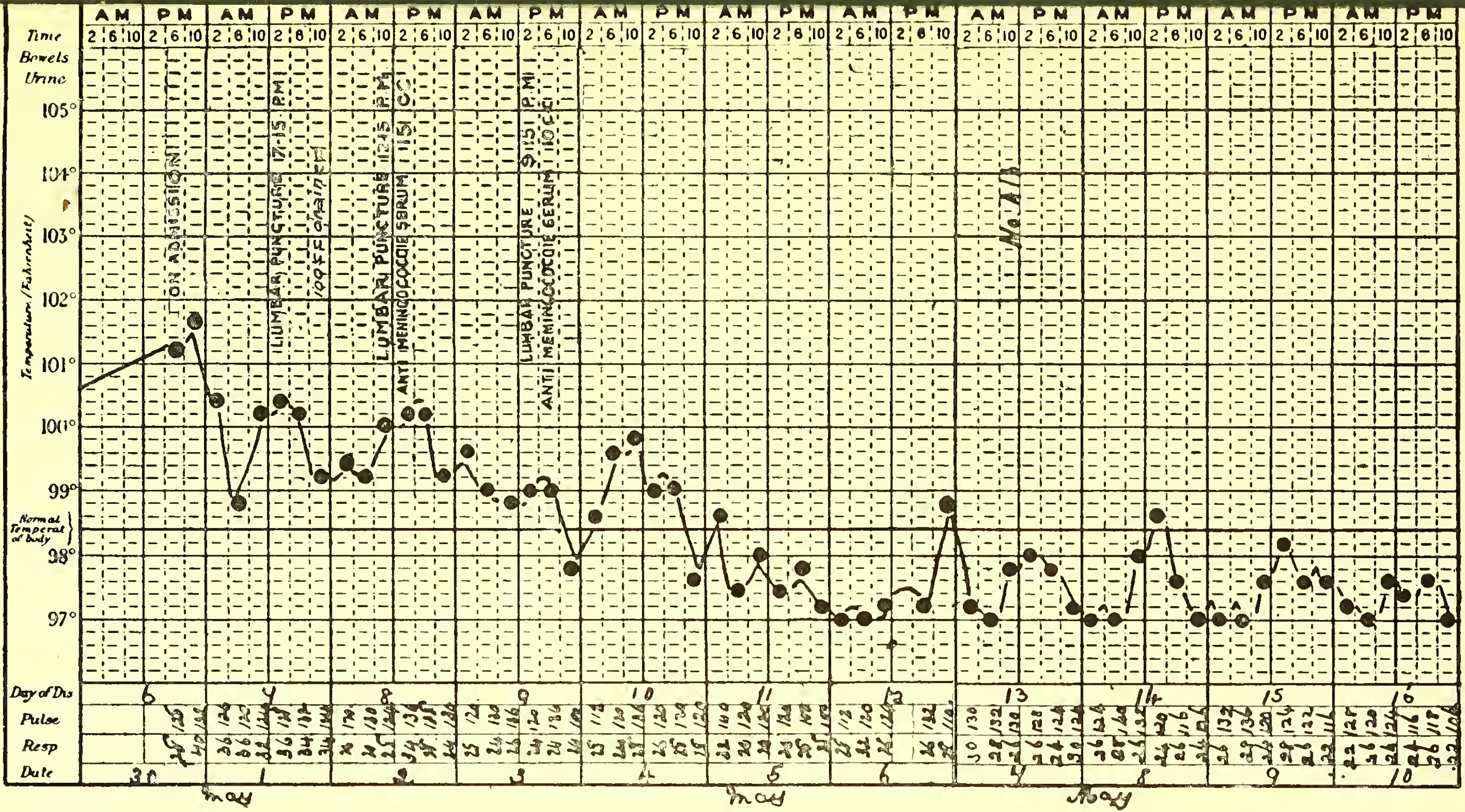

CHART 6.—Illustrating the abbreviation of an attack, and the lowering of the temperature, by lumbar puncture and the use of serum. The patient, a child of three years, was very ill, with marked retraction of the head. Many diplococci present in the cerebro-spinal fluid. Improvement began with simple lumbar puncture on seventh day. (From a case in Hornsey Fever Hospital under the care of Dr. Prior.)

of the serum injection should be remembered, and the temperature should be taken frequently during the first two hours after the procedure, so that the patient may be sponged or cradled if the temperature is high.

In a certain number of cases the fever becomes intermittent after the first week or two; this intermission is usually quotidian in type, but it may also be tertian (Charts 7 and 5). Some authors refer to cases running an intermitting temperature as a special type of the disease—the intermittent type. But as the symptom-complex in these cases is by no means constant or peculiar, the distinction seems unnecessary.

Occasional sharp rises of temperature are frequently seen in cases that appear to be gradually mending, when the original fever has subsided for several days. These *recrudescences* may last a few hours only, or one, two, or three days. They are often accompanied by a return of the headache, by insomnia and restlessness, or by an increase of the rigidity. Sometimes, however, no such appreciable set-back occurs at the time of the rise of temperature (see Chap. VI, § 1).

§ 7. **The Blood.**—The progressive anæmia present in all acute infective processes is present here also. No special value therefore attaches to the count of red cells nor to the hæmoglobin estimation. A marked leucocytosis occurs; in this respect the disease behaves like pneumonia and like other acute fevers due to pyogenic micro-organisms, but unlike typhoid fever and acute poliomyelitis, in both of which a leucopenia is

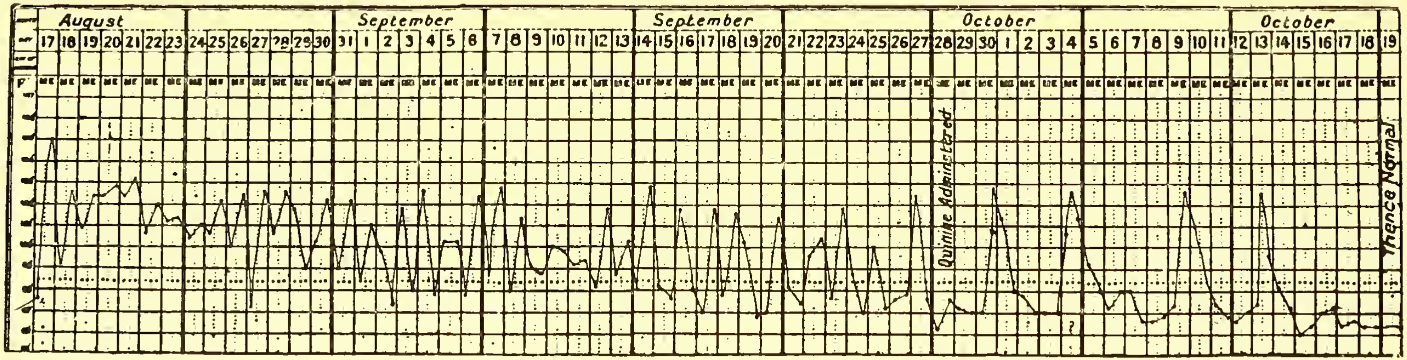

Chart 7.—Illustrating a prolonged case of cerebro-spinal fever in a young man, aged nineteen years. At the end of the seventh week, with temperature of the quotidian intermittent type, the use of quinine led to an irregular intermittence for the final ten days of the fever. (From a case under the care of Dr. Samuel West at St. Bartholomew's Hospital.)

present, and from both of which it is sometimes necessary to diagnose cerebro-spinal fever (see Chap. IX, §§ 4, 5). A common figure to find in cases of ordinary severity is 20,000–25,000; the writer has occasionally observed counts as high as 50,000–60,000. The meningococcus can often be isolated from the blood by culture during the first few days of the disease, if the case is of the superacute type; cerebro-spinal fever is therefore a general blood infection in its early stages, just as are pneumonia and typhoid fever. In the fulminating type positive blood-cultures are almost constantly obtained. In this form blood films that are taken and stained direct often show the specific coccus, and this fact is to be remembered as affording a possible means of rapid diagnosis.

§ 8. **The Urine.**—Several observers have confirmed a very early symptom noted by Tourdes: the occurrence of *polyuria* and of *polydipsia*. Polyuria accompanies the wasting, and is independent of the temperature: a patient who is febrile may still pass several litres of urine in the day. The condition is seen in children as well as in adults.

Albuminuria is not common and is rarely considerable in amount. *Hæmaturia* only occurs in cases with marked purpura. Transitory *glycosuria* is seen occasionally.

§ 9. **Sensory Disturbances.**—*Pains* are quite common at the onset of the disease, and may be referred to almost any part—a whole extremity, a single joint, the region of an orbit or behind the ear.

Headache is one of the cardinal symptoms and is rarely absent except in very mild cases. Its reference is often occipital, but in a great number of cases it is 'all over' the head. It may be so intense as to be quite intolerable, even by adults ordinarily capable of considerable control.

Hyperæsthesia is another common feature. It affects the special senses, producing photophobia and intolerance of noises, and the tactile sense, leading to supersensitiveness of the skin more or less universal.

Vaso-motor irritability is usually present—witness the flushing face and chest, and the presence of *tâches cérébrales*.

§ 10. **Eye Changes.**—1. Direct infection of the eye may take place:

(a) *Conjunctivitis* is not a common feature, but may occur, and the effusion may become purulent. Films made from the pus may show meningococci in characteristic fashion. In an epidemic studied by Norman Butler in East Africa purulent conjunctivitis was rather common.

(b) *Suppurative choroiditis* is much less common than conjunctivitis. Keratitis with hypopyon may complicate the condition.

2. Effects upon the nervous mechanism of the eye are much more common.

(a) *The pupils* are almost constantly dilated; it may be unequally so. This state of mydriasis is sometimes noticed to increase when the head is tilted forwards, as in testing the neck muscles for rigidity. It is also said to be increased at times during the demonstration of Kernig's sign. The light reflex is usually sluggish.

(b) *Strabismus* and *nystagmus* are not often present in adult cases, but are fairly common in children.

(c) *Optic neuritis* is not usual, even in cases that pursue a prolonged course. A transient papillitis is, however, said to be common at the period of most intense meningeal infection. The relative infrequency of changes in the optic disc in cerebro-spinal fever contrasts rather markedly with the high rate of incidence of optic neuritis in tuberculous meningitis.

§ 11. **The Knee-jerk and certain Reflexes.**—No general rules seem to apply to these physical signs in the disease, and the practitioner is advised to attach little or no value to them in arriving at a diagnosis. The *knee-jerk* is so often absent in severe cases of many acute general infections during the first few days (e. g. pneumonia) that its absence here gives no help. Indeed, the writer is of opinion that its presence is actually a slight point in favour of a diagnosis of cerebro-spinal fever in a doubtful case.

Equally variable is the state of the plantar response; *Babinski's sign* is often present, but it must be remembered that, like Kernig's sign, it is physiologically present in infants.

The *superficial reflexes* are usually preserved, unless the patient has sunk into a state of profound stupor or actual coma, when all reflexes are likely to be absent. But Michell Clarke observed that the abdominal reflexes were rather frequently absent in a small group of cases studied by him.

§ 12. **Stiffness of the Neck.**—Too much importance cannot possibly be attributed to this sign, and in the routine clinical investigation of every case of acute illness of doubtful nature *it should be carefully searched for at an early stage of the disease rather than be left to attract attention after it has become a marked feature.* It is probably the most constant of all the signs present, though it is doubtful if Kernig's sign does not share this distinction with it. It is probably present in a slight but in a definitely ascertainable degree very early in the disease. Its discovery, therefore, in the absence of such local causes as faucial angina and rheumatism is of the utmost moment, because this determines at once the question of lumbar puncture. Reference has been made (§ 2) to the fact that the patient commonly declines the supine position because this brings the occiput upon the pillow, and thus puts the muscles of the neck upon the stretch; whereas the lateral position allows the occiput to fall back and relaxes the affected muscles.

In all cases in which meningitis is suspected the neck must be examined carefully and critically by placing the occiput in the hollow of the hand and testing the movements of the head, especially that of dropping the chin forwards.

It is of value to remember that a very slight and doubtful degree of rigidity present at the beginning of this examination may become much more definite and unmistakable after a few movements are undertaken. Stiffness of the neck which is due to rheumatism, arthritis, or glandular enlargement commonly shows the contrary effect : to continue the examination diminishes the stiffness rather than increases it. The examination, therefore, should not be hastily abandoned as negative, but very thoroughly persisted in until it is certain that no stiffness exists. It must be remembered, too, that at an early stage of the disease the stiffness of the neck may be transitory : the examination should therefore be repeated at frequent intervals. If the patient is an adult, and is fully conscious, his statement that the manipulations are uncomfortable is in itself a suspicious thing, even in the absence of definite rigidity.

An early sign of the meningeal irritation is sometimes seen in the form of slight deviation of the head and neck to one side (Michell Clarke).

As the meningeal inflammation increases the rigidity becomes persistent and unmistakable and spreads to the rest of the spine, which becomes fixed and poker-like ; so that, in a child, the whole body can frequently be raised from the bed in a fully extended position by the hand placed behind the occiput.

Two further results of the increased rigidity of the neck and spine may be present : *retraction of the head* and *opisthotonus,* the whole spine being arched backwards so that the occiput and the sacrum form the extreme points of a curve with its convexity forwards. These two features are much more common in infants and younger children than in older children and adults. They are constant signs in the sporadic cases of meningococcus meningitis occurring in infants, and were originally designated, on account of this striking symptom, 'cervical opisthotonus of infants' (Gee and Barlow).

§ 13. **Kernig's Sign.**[1]—This sign is equally constant with neck rigidity and is of the same degree of importance as a diagnostic point. It is due to a slight stiffening of the hamstring muscles, resulting in the patient's inability to keep the knees extended if the hips are flexed to a right angle with the trunk. The small amount of 'slack' which is present in all muscles is 'taken up' during the meningeal irritation. The hamstrings form a convenient group of muscles in which to test this muscular tautness. If an attempt be made to bring the points of origin and insertion of the hamstrings closer together it is found that a state of painful stiffness is induced in them. Bearing in mind this rationale of the sign first described by Kernig, it follows that the test for it may be made in the following three ways:

(a) By raising the foot into the air whilst the knee is kept fully extended; as the hip becomes more and more flexed there is increasing difficulty in keeping the knee extended until, as the thigh approaches a right angle with the trunk, the maintenance of the extended position of the knee becomes impossible.

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[1] Originally described by Kernig in 1883, this very important clinical observation attracted little attention until Netter, in 1898, reasserted its extreme significance as a diagnostic point.

(b) By flexing the hip to a right angle, the knee also being flexed meanwhile; it will now be found impossible to extend the knee with the hip in this position without causing pain.

(c) By raising the shoulders from the bed, so that the trunk is bent at the hips; the legs will be drawn up into a position of flexion at the knees. This method of demonstrating Kernig's sign, though very striking, is only appropriate in children and in patients who are not gravely ill.

When present Kernig's sign is usually bilateral. But this is not always so; it is therefore necessary to examine each leg in turn.

All that has been said in the section on stiffness of the neck (§ 12) relative to the care spent in the examination applies equally to the search for Kernig's sign.

Kernig's sign is present as a physiological condition in infants up to the age of about two years; it is, therefore, without pathological significance until after this age.

§ 14. **Other rigidities** are less common, but well known. The abdominal muscles are often markedly contracted. Both Barnes and Michell Clarke noted the frequency of this feature in their cases. In some infants a tetanoid state of the extremities occurs. Trismus has been described.

CHAPTER VIII

COMPLICATIONS AND SEQUELS

The complications and sequels of cerebro-spinal fever will be considered in this order: (i) hydrocephalus; (ii) nervous complications; (iii) affections of the special senses; (iv) visceral complications; (v) sequels.

HYDROCEPHALUS

§ 1. **Mode of Origin.**—Reference has been already made to the anatomical points which bear upon this condition (Chap. IV, § 1). It must not be assumed that hydrocephalus is invariably due to mechanical closure of the foramina there described. Even in the post-basic type of the infection, where the plastic exudate is localized about the bulb and under surface of the cerebellum, there is evidence that the hydrocephalus which is so common a feature in the cases may arise without actual blocking of these orifices between the ventricles and the pia-arachnoid space. Two other possible explanations are—the total increase of fluid and of pressure in the ventricular arachnoid system, and the lack of mechanical resistance on the part of the ventricular walls. The first of these factors probably comes into play very prominently in those cases of hydrocephalus developing early in the meningitic process. The second factor is a very likely one in the hydrocephalus complicating the chronic infection in infants. Nor must it be forgotten that the ependyma of the ventricles is acutely infected in a good many cases, so that this tissue is softened by inflammation. Heiman refers to the possibility of the weight of fluid in the posterior horns of the lateral ventricles pressing down the cerebellum over the bulb and thus temporarily obliterating the outflow from the fourth ventricle.

§ 2. **Time of Appearance.**—Hydrocephalus may arise soon after the onset of the disease, as the result of the general rise in the amount and in the pressure of the cerebro-spinal fluid. Or it may develop, and often rather suddenly, in the course of the disease. Or it may be the final anatomical expression of the infective process, the counterpart of the symptom-complex seen in the chronic stage of the disease.

§ 3. **Symptoms and Diagnosis of Hydrocephalus.**—Hydrocephalus developing in the early stage of the disease is characterized by the features already described in the general symptomatology of the severe cases. Certain symptoms, however, are specially suggestive of the condition : pallor, cyanosis, increased frequency of the pulse with diminution in its tension and volume, shallow respirations, and stupor or coma supervening rather suddenly upon a previous state of consciousness.

If hydrocephalus arise at a later period of the disease than the end of the first week it may show itself with surprising suddenness, and sometimes in patients who seem to have been improving satisfactorily. In addition to the symptoms just enumerated there is a recrudescence of the headache, vomiting, and fever, which may have to a large extent subsided. More often it appears gradually, and concomitantly with the progressive cachexia of the chronic type of infection. A valuable sign of its presence in children and adults is the presence of a resonant note to percussion over the anterior horn of the lateral ventricle (Macewen). This sign is best obtained by placing the head in an upright position and inclining it to one side. The sign is not present in infants in whom the fontanelles are still open.

Hydrocephalus of the chronic stage of the disease is seen very constantly in infants suffering from the post-basic type of infection. But it is not uncommon in older children. Emaciation is a constant feature. The child lies for hours without stirring. There may be reiterated automatic acts, such as the biting of nails or the loosening and pulling out of teeth. The patients are rarely comatose. Vomiting and convulsions may occur. The clinical picture as seen in infants is described in Chap. VI, § 5.

§ 4. **Lumbar Puncture in Hydrocephalus.** When hydrocephalus develops early in the disease lumbar puncture usually yields a large quantity of thin fluid under considerable pressure. The relief to the symptoms by its performance is often immediate and striking. In hydrocephalus developing during the course of an acute case the result varies; sometimes there is a good deal of fluid, as in the early cases, but sometimes there is very little, with no increase in pressure. In the hydrocephalus of the chronic cases there is usually very little fluid, and there is no relief to the symptoms by its removal. Ventricular puncture, not lumbar puncture, is the therapeutic indication (see Chap. XIII, § 13).

NERVOUS COMPLICATIONS

Considering the delicate nature of the tissues that are inflamed in cerebro-spinal fever, and the intensity of the infective process in the majority of the cases, it is, as Netter and Debré remark, a somewhat surprising fact that the resulting effects upon the nervous system are relatively so few and of so temporary a nature. There have been times in the history of cerebro-spinal fever when good observers credited the disease with many more nervous complications and sequels than we now know to be due to it. The explanation of this fact lies in the confusion that for some time existed between the disease and poliomyelitis, of which infection paralyses of various parts are almost a natural consequence (see Chap. IX, § 5).

§ 5. **Psychic Disturbances.**—These are not very common, if the delirium and stupor are excluded. But the delirium may develop into mania, urged thereto by the violence of the headache. Periods of catalepsy have been noted in children. During convalescence it is not very uncommon to observe temperamental changes, such as puerility or emotionalism, which rarely persist for very long.

§ 6. **Motor Defects.**—Cranial nerve palsies are very uncommon. There are three groups of paralytic complications involving the limbs, all of them well authenticated, but none of them frequent in incidence.

(i) *Hemiplegia* and, less often, monoplegia of cortical type. This usually appears at the height of the disease, and is generally of temporary duration.

(ii) *Flaccid Paralyses* localized to one extremity or to a part of one extremity. These are apt to appear at an earlier stage of the disease than (i). Hyperæsthesia, or actual pain, in the affected limb may draw attention to the condition. The tendon jerks are lost. Muscular atrophy may ensue and R.D. may develop. Despite this degree of reduction, however, the prognosis for the limb is by no means bad, and complete, or almost complete, recovery is probable.[1] Lesser degrees of this type of paralysis, and more temporary in duration, are probably not uncommon. But they are not often looked for, owing to the natural desire to avoid much disturbance of the patient.

(iii) *Spastic ataxia.*—It is not uncommon to find convalescent patients very unsteady on their legs when they first begin to walk. Little children often refuse to walk at all for a time, even if they had learnt to do so before the illness began. Older children sprawl about the floor. Adults tend to topple over in an indiscriminate manner. In the majority of these cases there are no signs of organic disease, and the return to a normal gait is only a matter of time. In a few of the cases, however, the ataxia is accompanied by exaggerated knee-jerks, true ankle clonus, and extensor plantar response: a state of spasticity. The sphincters are intact and there is no anæsthesia or analgesia. According to Sophian, who draws attention to these cases, the pupils often remain dilated, with a sluggish light reflex. Recovery, though slow, is the rule.

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[1] A much more benign sequence than is to be expected in the cases of poliomyelitis, from which these cases of cerebro-spinal fever with flaccid palsy of an extremity have sometimes to be diagnosed, and in which permanent paralysis is the customary result. The difference in prognosis is, of course, due to the difference in the situation of the causative lesion: in cerebro-spinal meningitis this is in the nerve-root as it passes out from the cord in its pia-arachnoidal sheath; in poliomyelitis it is in the anterior horn-cells.

§ 7. **Sensory Disturbances.**—There is little or nothing to say under this heading. Exacerbations of the headache, marked hyperæsthesiæ, and severe pains in the limbs or elsewhere, have been referred to under the symptomatology. Netter refers to the occurrence of severe sciatic pain which may persist during convalescence.

Special Senses

§ 8. **The Eye.**—Complications involving this organ are very variable and yet, in relation to the essentially nervous character of the main lesions of the disease, they are not very common. Fortunately, with the single exception of that form of blindness so often seen in the recovered cases of the post-basic type of the disease, very few of the eye complications are permanent. The same grouping as was adopted in the description of the eye symptoms (Chap. VII, § 10) will be followed here :

(i) *Inflammatory lesions.* These are due to infective processes arising either directly from the nasopharynx by way of the lachrymal ducts, or indirectly through the blood-stream. *Conjunctivitis* is more common in some epidemics than in others and, if it occurs in severe degree, may be accompanied by *keratitis. Iridocyclitis,* most often unilateral, is less common but is very serious when present, because it leads to a suppurating ophthalmitis and destruction of the eye. *Cellulitis of the orbit* has been noted rarely. Netter and Debré describe a case with bilateral thrombosis of the cavernous sinus and double orbital inflammation.

(ii) *Nervous lesions. Intrinsic ocular defects,* other than the mydriasis which is so constant a feature of the disease, are so rare as to be curiosities. *Extrinsic defects* are not uncommon, but they are generally transitory (i.e. spasmodic). VI is, as usual, most frequently involved, then III. True paralytic strabismus (again generally VI, leading to external squint) is much less common in cerebro-spinal fever than in tuberculous meningitis. It usually passes off with convalescence. *Amaurosis* is relatively common in the post-basic infection of infants ; it is fortunately unusual in the more acute infection of children and adults. It is in most cases unaccompanied by any changes in the optic disc, and is therefore to be attributed to cortical changes associated with hydrocephalus. In some cases, however, a state of secondary optic atrophy is present. *Optic neuritis* is not a common complication, but *papillitis*, or a lesser degree of change even than this, is said by French authors to be extremely common. Here, again, it is difficult for English observers to judge of the actual facts, because the daily systematic use of the ophthalmoscope does not obtain with them once the diagnosis is made, owing to the disturbing effect upon the patient.

§ 9. **The Ear.**—(i) *Middle-ear disease* is strangely uncommon when the proximity of the naso-pharynx is remembered. Mastoiditis does not appear to occur at all.

(ii) *Meningitic deafness.* This is a common and very serious complication, serious because when it occurs it is apt to be permanent. The mode of origin of the deafness is probably by direct extension of the inflammatory exudate along the arachnoid sheath of VIII. The auditory defect generally begins early in the course of the disease, and usually before the end of the first week. It is usually bilateral, which adds to the seriousness of the trouble in the event of its becoming permanent. Both bone and air conduction are lost.

Visceral and Serous Membrane Complications

§ 10. **Arthropathies.**—A certain degree of painful stiffness, and even swelling of the joints, is not at all uncommon in cerebro-spinal fever. It is transitory as a rule. Occasionally, however, one joint shows evidence of much more intense infection, becoming red, swollen, and very painful with the slightest movement. It may suppurate, in which case it is important to remember the possibility of a secondary infection. In a patient seen by the writer with Dr. Lunn at the North-western Fever Hospital a copious growth both of meningococcus and of staphylococcus aureus was obtained from the pus removed from the joint by puncture. The large joints are more apt to suffer than the small ones. Unlike the arthritis of gonococcus infections, the involved joints do not give much trouble after the general infection has subsided: residual pains, adhesions, and anchyloses are rare.

The existence of marked arthritis in a case of cerebro-spinal fever may lead to a diagnosis of rheumatic fever (see Chap. IX, § 4). But a still greater difficulty may arise when the arthritis appears with little or no fever or symptoms of a severe infection. Such instances of mild meningococcus infection with a disproportionate degree of joint involvement are uncommon, but it is necessary not to lose sight of their existence when faced with a case of subacute arthritis, especially during the wane of an epidemic of cerebro-spinal fever.

The *arthritis due to serum administration* must be distinguished from that due to the meningococcus infection. The former appears, if it appears at all, with great constancy about the seventh to the tenth day after administration of the first dose of serum, and is generally associated with an urticarial rash. The condition is usually an arthralgia rather than an arthritis, the pain being disproportionate to the amount of inflammation in the joint.

§ 11. **Pulmonary Complications.**—Reference has been made (Chap. VI, § 6) to the onset of cerebro-spinal fever with *broncho-pneumonia* in little children. It is not a very unusual occurrence. Lung puncture in one such case observed by the writer yielded pneumococci only. But the meningococcus has been isolated from the sputa in some cases of *pneumonia*, in addition to pneumococci. Heiman reports a case in which meningococci were cultivated from the blood-stream as well as from the cerebro-spinal fluid and in which lobar pneumonia was definitely present. Lung puncture was not performed. No doubt most of these cases are mixed infections. Pleurisy only seems to occur as part of a pneumonia. Pulmonary complications appear to have been very common in some of the earliest recorded epidemics of the disease.

§ 12. **Various.**—Sophian found *pyelitis* present in 5 per cent of the cases studied by him in the Texas epidemic of 1912—another instance of the variability of particular affections in different epidemics, for few other authors mention this complication. In Sophian's cases the urine was purulent and contained many intra- and extracellular meningococci. The pyelitis may arise during convalescence.

Phlebitis has occurred. *Cardiac complications* are conspicuous by their absence, apart from the endocarditis which may accompany true meningococcus septicæmia.

Gastro-intestinal disturbances have little significance apart from the vomiting which is so constant a feature of the disease, and the diarrhœa which is not infrequently present with the invasion symptoms in infants and little children.

SEQUELS

§13. The three morbid conditions with which a certain number of the recovered cases of cerebro-spinal fever are left are psychic disturbances, deafness, and blindness.

(i) *Psychic changes.* French authors have noted these sequels more frequently than others. They describe conditions of irritability, of anger, and of puerility; of marked loss of attention or of memory. More subtle changes in character may occur—patients may be morbidly shy or morbidly egotistical. Secondary dementia is not unknown. It has been estimated that some 3 per cent of idiots owe their mental defect to an attack of cerebro-spinal fever (Looft). For the most part, however, these psychic changes following the disease disappear after a variable time. Such is not the case, unfortunately, with—

(ii) *Deafness,* if this is still present during convalescence. It is usually a permanent and incurable affair. There is great divergency in the statistics on this point, the number of acquired deaf-mutes who owe their defect to cerebro-spinal fever being variously estimated at 20 to 30 per cent (Gassot).

(iii) *Blindness,* as already observed, is not nearly so common as deafness, either as a complication or as a sequel. But if hydrocephalus has persisted for some time it may remain as a permanent defect in cases that slowly recover from the disease.

CHAPTER IX

DIAGNOSIS

§ 1. **General Remarks.**—With a disease so protean in its manifestations it is not surprising that frequent errors should arise in diagnosis, as indeed they not seldom do. The chief difficulty lies in not suspecting the presence of the disease. If the possibility of it occurs to the mind of the practitioner in connexion with any particular case it is not common to be unable to arrive at a definite conclusion. It is, of course, much more easy to bear in mind the possibility of cerebrospinal fever during the presence of an epidemic than at other times. This is the reason why the cases which go undiagnosed, at least during the first part of their course, are more often those sporadic cases which happen to be atypical.

§ 2. **Meningism.**—The reason why it may not be possible to decide on clinical grounds whether meningitis is present or no is because several infective processes, other than that due to the meningococcus, are apt to produce symptoms highly suggestive of meningeal irritation. This state of meningeal irritation, when due to toxæmia and not due to actual meningitis, has been termed meningism or meningismus. The question whether such a state is entirely toxic, or whether it is due to definite though slight changes in the meningeal tissues which just stop short of an inflammatory exudate, is problematical. It is not unlikely that a good many of the endotoxins of the acute specific fevers are capable of producing changes in the pia-arachnoid and in the grey matter immediately beneath it, without leading to actual meningo-encephalitis. The clinical representative of such toxic changes is the condition we term meningism. These remarks should be read in conjunction with those in Chap. IV, dealing with the characters of the cerebro-spinal fluid in health, and the changes undergone by it in various grades of toxicity and in definite meningitic infection.

The diagnosis of cerebro-spinal fever may be conveniently considered under three heads: (i) from various acute infective processes with toxæmia, leading to ‘cerebral’ symptoms; (ii) from certain acute cerebral diseases, of primary origin; (iii) from other forms of meningitis.

§ 3. **The Diagnosis of Meningitis from Toxæmia merely.**—It will now become obvious that in a large number of cases of acute illness of doubtful nature, the first question of fundamental importance is this: is the patient suffering from meningitis? The question is settled partly by the clinical data and, if these are not definitely negative, partly by an examination of the cerebro-spinal fluid obtained by lumbar puncture.

In making the distinction between meningitis on the one hand and toxæmia on the other, in a case of fever with ‘head symptoms’, the following differential points should be borne in mind. It is well to consider them individually in every doubtful case.

(i) *If headache and delirium synchronize, meningitis is probably present, and not merely toxæmia.* Contrast an ordinary case of typhoid fever (toxæmia), in which headache and delirium alternate, the patient being free from pain when he is delirious, with cerebro-spinal fever (meningitis), in which the patient's headache and delirium are both present at the same moment: he is often delirious about his headache. This is an old distinction, attributed originally to Sir William Jenner, and it is one of great value. It is not, of course, available in infants and little children, because in these patients neither headache nor true delirium is present. But in older children and in adults the distinction gives very valuable information.

(ii) *Vomiting.* If this occurs, not merely at the onset of the fever, but on subsequent days also, at a time when the invasion period of the infection may be said to be passed, it is evidence of meningitis.

(iii) *Pulse and respirations.* Irregularities in rhythm are in favour of meningitis, and so is a relatively low pulse-rate in comparison with the height of the temperature, provided typhoid fever can be eliminated.

(iv) *Stiffness of the neck* without signs of otitis, enlarged glands, or of other local inflammation, even though it only exists in slight degree, is strongly in favour of meningitis. If the stiffness increases, rather than diminishes, with prolongation of the examination, the presumption is still greater.

(v) *Kernig's sign*, provided the patient is over two years of age, may be taken as being of equal significance with stiffness of the neck.

(vi) *Optic neuritis*, though its presence is much in favour of meningitis as against toxæmia merely, is not of much value in this connexion, because it is usually absent at the early stage of the disease when the diagnostic problem requires urgent solution.

These six points are worthy of the most critical investigation. All other clinical features that may be present are equivocal—they may be produced by a toxic state of the brain or meninges. This statement refers to the state of the pupils, whether contracted or dilated; the presence of *tâches cérébrales*; the absence of the superficial or of the deep reflexes; the 'peevish' state of the patient with a resistant attitude; marked insomnia or persistent stupor.

The most difficult cases of all are those in which meningitis is present and yet few (or it may even be none) of the distinguishing symptoms of the disease are shown by the patient.

§ 4. **Acute Infective Processes with Toxæmic Symptoms simulating Meningitis.**—Almost any of the acute specific fevers may behave in this manner.

(i) *Influenza.* This is mentioned first because it gives most difficulty in actual practice. The seasonal incidence of influenza and cerebro-spinal fever is likely to be the same ; the occurrence of both diseases at the same time of year is therefore confusing. *It should be noted that cerebro-spinal fever is very often mistaken for influenza, whereas influenza is rarely mistaken for cerebro-spinal fever.* The reason for this lies in the fact that the diagnosis of influenza is too often by exclusion. A patient falls suddenly ill with fever, headache, and pains in the back and limbs. There are no obvious physical signs. A provisional diagnosis of influenza is made, largely because the friends demand some definite expression of opinion as to the nature of the malady, when in reality no definite pronouncement can be made.[1] As the days pass there is a danger that the practitioner may fail to keep clearly before him the fact that his diagnosis of influenza is tentative only ; he may himself be led insidiously to regard the case as of this nature, and thus the patient may be deprived of the benefit of that divine discontent on the part of his attendant which is of such inestimable value in the conduct of a case of doubtful nature. Then comes the awakening, with the appearance of active delirium associated with the headache; or stupor; or some other serious manifestation which the practitioner properly hesitates to attribute to influenza simply. No doubt the awakening does not come at all in some of those cases that escape recognition: the patient recovers from a mild attack of cerebro-spinal fever, convalesces slowly (confirming the notion that his malady was influenza), and no one is any the wiser. The error should, of course, be avoided whenever possible; in the severe case the loss of time before the administration of serum may prove a most serious handicap to recovery; in the mild case a source of danger to the community may arise in the non-recognition of the nature of the infection. *Fever prolonged past the seventh day, in the absence of an inflammatory focus (bronchitis, pneumonia, pleurisy, sinusitis, &c.), is unlikely to be due to influenza, and should therefore lead to a critical revision of the diagnosis.*

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[1] Definite criteria of a positive sort are still unavailable in regard to the diagnosis of influenza, and bacteriological investigations do not always help, because it is extremely probable that different 'influenza' epidemics have different causative micro-organisms associated with them. At present there is no general consensus of opinion that only those epidemics or cases associated with Pfeiffer's bacillus should be termed influenzal, and experience justifies this hesitancy, despite the fact that the absence of some definite bacteriological criterion renders diagnosis extremely difficult.

(ii) *Typhoid fever.* The onset of the illness is nearly always a gradual one, and the evolution of the toxic symptoms is much more deliberate than in cerebro-spinal fever. This is perhaps the most significant differential point clinically. The leucocyte count is very helpful, and may prove of great diagnostic assistance before Widal's test is available: the count is low in typhoid (2,000–7,000), but it is high in cerebro-spinal fever (15,000–40,000). The rose spots of typhoid do not appear until the eighth or tenth day, whereas the rash of cerebro-spinal fever which might be confused with these usually appears much earlier. If the spleen is palpable in cerebro-spinal fever it is so early, whilst the disease is at its 'septicæmic' stage; in typhoid the spleen can rarely be felt before the end of the first week. The dis-association of headache and delirium in toxæmia, referred to under § 3 of this chapter, is strikingly seen in typhoid fever. Moreover, the disappearance of the headache altogether, which occurs so frequently in typhoid fever after the tenth day, is another point of distinction: although its severity may diminish, it is rarely absent so early in the course of cerebro-spinal fever.

As soon as a positive Widal test is obtained (usually about the seventh to tenth day), this finding, together with a leucopenia, may be relied upon as decisive in favour of typhoid. A positive blood-culture may often be obtained before the agglutination test is available.

(iii) *Pneumonia.* Acute pneumococcus infection is the most common cause of a toxæmic state leading to meningism; the patient is usually a child, but not always. The symptoms of meningeal irritation may precede the signs of pulmonary disease, in which case the diagnosis can only be settled by lumbar puncture, or they may concur with such signs, in which case some care must be exercised lest the case be one of cerebro-spinal fever ushered in by pneumonia (see Chap. VI, § 6). Here the leucocyte count is of no help, for there is a high leucocytosis in pneumonia as in cerebro-spinal fever. A blood-culture may reveal pneumococci, or a lung puncture may yield direct evidence of the nature of the infection ; but if the diagnosis is considered in serious doubt, it will probably be deemed wise to perform lumbar puncture.

(iv) *Measles.* The differential diagnosis between this disease and cerebro-spinal meningitis does not appear to be a matter of practical difficulty. But in the writer's experience, although no reference is made to the fact by authors, it is sometimes necessary to decide whether or no a mixed infection is present. The specific toxin of measles is undoubtedly able to exercise a selective action upon the cerebro-spinal system, producing a clinical picture which, especially in the presence of an epidemic of cerebro-spinal fever, may easily lead to difficulty. There is good evidence that acute encephalitis may occur as an immediate sequel to measles. The writer has seen two adult patients in whom this particular difficulty arose ; cerebro-spinal fever and measles were both epidemic at the time. The cerebral symptoms developed suddenly, in one case twenty-four hours, in the other forty-eight hours, after the fall of the measles temperature. Analysis of the available data led to the conclusion that in one case there was a mixed infection of measles and meningococcus, and that in the other the condition was due to measles only. Chart 6 illustrates the abrupt onset of a straightforward attack of cerebro-spinal fever on the fourth day after measles in a schoolboy. Measles was epidemic in the school at the time, and there were numerous cases of cerebro-spinal fever in the neighbourhood. The boy in the next bed also developed cerebro-spinal fever ten days after the first; these were the only two who developed cerebro-spinal fever out of thirty cases of measles in the school.

(v) *Malignant small-pox,* on the authority of Milligan, simulates cerebro-spinal fever very closely, on account of the sudden onset, headache, vomiting, and pain in the back. But as the eruption occurs on the third or fourth day the diagnosis is not left long in doubt.

(vi) *Rheumatic fever.* If cerebro-spinal fever begins with arthritis and profuse acid sweats, if the patient is an adolescent, and if the pains are specially referred to the joints, the diagnosis of rheumatic fever is at first pardonable. The addition of an erythema makes the simulation all the closer. The failure of salicylates to relieve the pain, or to reduce the fever, should at once arouse suspicion. The important distinction between early rigidity of the neck in meningitis, and rheumatic stiffness—that the former tends to increase with examination and the latter tends to decrease—should be remembered in this connexion.

§ 5. **Differential Diagnosis of Cerebro-spinal Fever from certain Diseases of the Central Nervous System.**—The most important of these diseases sometimes introducing a difficulty is—

(i) *Poliomyelitis* (*infantile paralysis*). This disease, like cerebro-spinal fever, exists in epidemic and in sporadic forms. Of recent years there have been several small epidemics in England. The most conspicuous of these occurred in Devon and Cornwall in

1911. Sporadic cases are very common. If the type of the disease is the usual one little or no difficulty is introduced in diagnosis from cerebro-spinal fever, because the invasion or febrile stage is short and the degree of illness it involves is not great ; it is quickly followed by the paralytic stage, and the real nature of the malady becomes manifest. In the cerebral type of poliomyelitis, however—the acute polio-encephalitis of Strumpell—there may be some resemblance to cerebro-spinal fever in that the patient often lies in a state of semi-stupor, and vomiting may occur and may persist for two or three days. It is, however, in the meningitic form of the disease, originally described by Wickman, that a real difficulty presents itself. There may be added to the headache and vomiting, pain and stiffness in the neck and spine and even some degree of opisthotonus. It is considered by those who have recently carried out experimental work with the virus of poliomyelitis that the pia-arachnoid is not infrequently involved in the disease-process. So closely did some of these cases of poliomyelitis resemble cerebro-spinal fever that it was even suggested at one time that the two diseases were identical. The number of cases of poliomyelitis occurring in this meningitic form varies in different epidemics. Netter found them as high as 29 per cent. in the cases studied by him (quoted in Romer's monograph, translated by Prentice). The difficulty in diagnosis is increased by the fact that herpes is not uncommon in acute poliomyelitis.

According to E. Müller, the febrile stage of poliomyelitis is accompanied by a leucopenia. And some importance should be attached to the fact that cases of poliomyelitis are at the height of their curve of incidence in August, whereas cases of cerebro-spinal fever occur most frequently in the winter and early spring. But it is obvious that with such close resemblance as may transpire between the clinical picture in the two diseases, nothing less than a study of the lumbar puncture fluid may settle the diagnosis in a doubtful case (Chap. IV, § 7).

(ii) *Epilepsy.* The writer has seen a child in a state of epileptic stupor, of four days' duration, with raised temperature, and with doubtful Kernig's sign, in whom it was not possible to exclude meningitis, and therefore advisable to perform lumbar puncture.

Meningism may occur in a child as the result of acute gastric or intestinal irritation, and especially as the result of *Ascaris lumbricoides.*

§ 6. **Differential Diagnosis of Meningococcus from other Forms of Meningitis.**

(i) *Pneumococcus meningitis* is rarely primary; almost always it complicates consolidation of the lung, or pleurisy, or otitis media, or infection of the nasal sinuses. But when it occurs it is apt to be extremely acute, running a rapid course and nearly always a fatal one.

(ii) *Streptococcus meningitis* usually complicates some infective process about the skull, and most often this is middle-ear disease or sinusitis. In the majority of cases some surgical procedure has been attempted for the relief of the primary condition.

(iii) '*Influenzal' meningitis* is a term applied somewhat loosely. The knowledge imparted by lumbar puncture has caused most practitioners to hesitate to diagnose influenzal meningitis from clinical grounds alone. And it is a striking fact that those cases in which Pfeiffer's bacillus is isolated from the lumbar puncture fluid, with the exudate of an acute meningitis, and definite symptoms, are not usually cases in which influenza has been suspected, still less diagnosed.[1] What most often happens is that a patient presents symptoms of meningitis of an acute kind, a lumbar puncture is performed, and the influenza bacillus is demonstrated in the cerebro-spinal fluid.

(iv) *Typhoid meningitis.* A true infection of the meninges may occur in typhoid fever, but it must not be inferred that a patient necessarily has typhoid meningitis because the bacillus is grown from the lumbar puncture fluid. This may occur without clinical evidence of meningitis and without histological and chemical changes in the cerebro-spinal fluid characteristic of meningeal inflammation (see Chap. IV, § 4, and foot-note).

(v) *Tuberculous meningitis.* This is by far the commonest form of acute meningitis and therefore deserves fuller mention. The most helpful points in a differential diagnosis from meningococcus meningitis are the following. Tuberculous meningitis is rarely so sudden in its onset, the meningitic symptoms being preceded by a longer period of malaise, which begins less abruptly than the invasion symptoms of cerebro-spinal fever. The temperature is seldom high, except as an ante-mortem event, the usual range being 99°–101°. Retraction of the head is transient and ill-marked, or is absent. Photophobia is common, whereas it is quite uncommon in cerebro-spinal fever. Netter and Debré attach great importance to this point, and these authors consider the optic disc usually remains free from changes in tuberculous meningitis, whilst in meningococcus meningitis it frequently shows papillitis. In adults aphasia is often a common and an early symptom. True (paralytic) squint is common. The 'peevish' condition in children is much more marked during the first week. In both children and adults the depth of stupor after about the tenth day is much greater. The discovery of tubercles in the choroid is pathognomonic, but these lesions rarely appear before the third week of the disease, and are therefore not of much service for diagnosis. Some authors lay stress upon the presence of signs of tuberculous disease elsewhere in the body as assisting in the diagnosis, but this is, of course, not true. Except in the case of adults, and by no means always then, there are very rarely any such signs: the source of the disseminate tuberculosis is a softened caseous gland, bronchial in the great majority of cases, mesenteric in a few; and the child usually gives no sign of this focus, nor of any other. The leucocyte count affords no differential help as from cerebro-spinal fever, a leucocytosis of considerable size (15,000–30,000) being present in tuberculous meningitis.

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[1] It is so with the cases of endocarditis in which Pfeiffer's bacillus has been isolated by blood culture—they are not usually cases in which symptoms of influenza have been present.

However high a degree of probability the result of a general examination may yield that a patient is suffering from meningitis, confirmation of this view rests entirely upon the results of lumbar puncture. For three reasons it should not be deferred: it establishes the diagnosis that meningitis is present; it decides the nature of the infection; it is a valuable aid to treatment in the event of a positive result. The differential points found on examination of the cerebro-spinal fluid in other forms of meningitic infection are detailed in Chap. IV, § 6.

CHAPTER X

PATHOGENESIS

§ 1. **The Causative Agent.**—Some reference must now be made to the question of the essential ætiological factor in cerebro-spinal fever, although the identity of the meningococcus with the *materies morbi* of the disease has already been assumed in the foregoing chapters. The argument leading to the conclusion that the meningococcus is the essential cause of cerebro-spinal fever is fully as complete as is the argument in the case of any other specific infection of which we have knowledge, and it is much more complete than in many infections. That the diplococcus of Weichselbaum is the *sole* cause of the disease must be premised until some other agent is brought forward concerning which substantial data are adduced in favour of its causative action. For the purpose of this brief discussion ‘ some other agent ’ may be taken to include a hypothetical microbe in the life-history of which the meningococcus, as usually described, represents a non-infective stage, as well as a hypothetical microbe having no biological relationship with the diplococcus.[1]

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[1] No bacteriological work can be considered to contravene the generally accepted view here taken of the causative nature of the meningococcus if it falls short of that exactness which is essential to such investigations. The doctrine of the ‘ pure

Weichselbaum's diplococcus fulfils all Koch's postulates, and more. The meningococcus is obtained from all cases of the disease, making allowances for technique that are regarded as reasonable in all other specific infections ; it can be grown outside the body in pure culture ; it is not found in association with the lesions of other morbid processes ; it is capable of producing the disease when injected into susceptible animals and it can be recovered from the lesions so produced and again cultivated outside the body. More than this, it is agglutinated by the serum of patients suffering from the disease, it yields the complement-fixation test, and it may be utilized to prepare an immune serum which is curative in its properties if brought into direct contact with itself during the infective stage of the disease.

If all these facts are allowed, there is no room for doubt as to the causative action of the meningococcus ;

culture ' must be insisted upon throughout, and it is wiser to reserve the publication of researches that cannot be expressed in terms of this doctrine for fuller analysis. As an example of the kind of statement which only serves to confound knowledge the writer chooses the following, taken from a recent contribution to the bacteriology of the disease by authors who are sceptical of the causative rôle of the meningococcus :

' Stained films from the central bluish haze, in which the colonies were too small to be seen with the naked eye, showed

(*a*) Gram-negative diplococci indistinguishable from the meningococcus of Weichselbaum;
(*b*) Slender Gram-negative bacilli ;
(*c*) Gram-negative "biscuit-bacilli" ;
(*d*) Gram-negative and Gram-positive diplo-bacilli. . .

Attempts to isolate individual types (*a*), (*b*), (*c*) by the method of dilution failed. . . .'

certainly there is no room for doubt if it be admitted that these facts are linked together in causal association. But, although the bare facts cannot be disputed, there are some authors who are unconvinced, and who explain these facts as being fortuitous and as lacking essential significance. Thus, it is pointed out that other micro-organisms than the meningococcus are capable of producing cerebro-spinal meningitis in monkeys, which is quite true: reference is made in various sections of this book to the fact that there is nothing specific in the symptoms or in the post-mortem findings of meningococcus meningitis; but where nothing specific is produced by the action of a micro-organism in nature nothing specific must be expected by experiment. It suffices that the injection of the meningococcus into the spinal theca of susceptible animals leads to a series of nervous symptoms, to death, to lesions found post mortem which are identical with those of cerebro-spinal fever in man, and to the isolation of the meningococcus from these lesions, from the blood, and from the mucosa of the naso-pharynx. The work of Lingelsheim, Kolle and Wassermann, Dopter and Flexner admits of no other interpretation. Again, the curative action of the immune serum is doubted because some other methods of treatment are occasionally successful, because some cases of the disease recover without treatment at all, and because others die despite serum administration—arguments that are still applied by anti-vivisectors to prove that diphtheria antitoxin is not curative in diphtheria. In this discussion it is not single facts that count, but the combination of facts. Any one of the series of remarkable discoveries connected with cerebro-spinal fever that began with the recognition of the diplococcus by Weichselbaum may be so criticized as to produce scepticism concerning its exact interpretation, but no one with a judicial mind, and no special knowledge of medicine, could pass in review the whole of the evidence without concluding that the meningococcus is the sole essential causative agent of cerebro-spinal fever.

The chief objections to the acceptance of this view arise more from the difficulties of explaining the epidemiological facts, perhaps, than from a refusal to acknowledge the bacteriological, pathological, and clinical data.[1] These difficulties have been discussed in Chapter II. A full recognition of the rôle played by the 'carrier' offers, as there stated, a rational solution to the epidemiological difficulties.

§ 2. **Route of Penetration of the Body by the Meningococcus.**—That the initial site of entry of the coccus into the body at the time of infection is the naso-pharynx all authorities are agreed. But the manner by which the meninges, the tissues of election of the coccus, are reached, is still open to considerable debate. There are two main routes of entry, (i) the

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[1] 'He questioned whether the various organisms described played any more important part than that of secondary invaders' (W. H. Hamer, quoted from Report of Discussion on Epidemiology of Cerebro-spinal Meningitis, *Brit. Med. Journ* March 13, 1915).

direct route, from the naso-pharynx through some adjacent structure to the arachnoidal tissues at the base of the brain, and (ii) the *indirect route,* from the naso-pharynx to the blood-stream and thence to the meninges.

(i) *The direct route.* Three possible channels exist. (*a*) Through the middle ear, by way of the Eustachian tubes; thence to the internal ear and along the extension of the pia-arachnoid sheath of the auditory nerve. The relative rarity with which otitis media is found in cerebro-spinal meningitis, and the lateness in the course of the disease in which, when it does occur, it appears, seem powerful arguments against this view. (*b*) Through the sphenoidal sinuses and the sphenoid bone. The early work of Westenhoeffer pointed to this route as being the most probable one. This observer found the sphenoidal sinuses to be affected in a number of cases carefully examined post mortem, and was perhaps also influenced by the knowledge that the exudate first to appear lies at the base of the brain close to the basi-sphenoid. But this latter observation cannot be said to help in the determination of the route of entry of the coccus, because a similar site of election of the inflammatory exudate is seen in tuberculous meningitis, a disease in which it is clear that the bacillus arrives in the pia-arachnoid tissue *via* the blood-stream. As a matter of fact, Westenhoeffer's later observations led him to abandon this view of the sphenoidal route, because these further researches failed to demonstrate the meningococcus in the bone itself, and showed that the exudate was confined to the superior and lateral aspects of the sphenoid. Westenhoeffer's original theory has been re-stated more recently, however, by other observers, some of whom have succeeded in demonstrating the coccus in the bony tissue (Embleton and Peters). (*c*) The trans-ethmoidal route. This mode of entry of the meningococcus into the pia-arachnoid tissue is favoured by Netter and Debré, who advance strong arguments in favour of it. They point out that, in addition to the prolongation of the pia-arachnoid membranes which ensheath the nerve filaments passing from the olfactory bulb through the cribriform plate of the ethmoid, there are definite extensions of the pia-arachnoid space through the ethmoid, analogous with similar extensions in the internal ear and around the optic nerve. These pia-arachnoid extensions communicate with the sub-mucous lymphatic channels of the nasal fossæ. By means of injections of methylene blue and of Chinese ink into the pia-arachnoid space of the dog or rabbit, a current can be demonstrated from this situation to the lymphatics of the naso-pharynx. The meningococcus, similarly injected in monkeys, finds its way also to the naso-pharynx. Netter and Debré postulate a reverse current taking place when a patient develops meningitis by the meningococcus reaching the membranes of the brain from its initial nidus in the mucosa of the nasal fossæ. The extra permeability of the canaliculi above described in infants would account for their special liability to develop cerebro-spinal fever, and the partial obliteration of the channels in adults would explain their relative immunity to the disease.

The main difficulty in accepting either of these direct routes as being the natural mode of penetration is the lack of experimental proof. Infection of the meninges has not yet been produced in animals by the injection of the meningococcus into the nasal fossæ. The fact that Flexner was able to produce poliomyelitis by intranasal inoculation of the virus of the disease in monkeys, and to prove that the infection of the olfactory lobes occurred directly and without an intermediate blood infection, is of interest in this connexion.

(ii) *The indirect route by the blood-stream.* This is the mode of invasion of the pia-arachnoid tissues that commends itself to most observers. But it must be confessed that most of the arguments adduced in its favour can be accorded a different interpretation. On clinical grounds the suddenness of the onset of most cases of the disease favours this view of infection of the meninges. Elser and Huntoon refer, by way of contrast, to the gradual onset usually seen in meningitis secondary to otitis media. But it might well be argued that there is no certain knowledge that the last-named form of meningitis itself spreads directly from the ear rather than develops after blood infection. The data afforded by blood culture do not settle the matter. Although positive blood cultures are by no means uncommon in the early stage of the disease, they are certainly not obtained in more than 25 per cent of the cases. The existence of cases of meningococcus septicæmia, well proven though these are, helps very little, because these cases are different in nature from ordinary cases of cerebro-spinal fever: in some of them, as in Andrewes' case, there is no meningitis at all. Meningococcus septicæmia has no necessary relation to meningococcus meningitis, either in its mode of production, its clinical features, or its treatment. That evidence of blood infection occurs after the first few days—in the existence of arthopathies, &c.—is, again, no proof of the original mode of entry into the meninges being by the blood-stream, because the blood infection may well be secondary to the meningitis. More significant is the occurrence of cases in which a meningococcæmia is proved to exist for some days before any evidence of meningitis is forthcoming; but such cases are rare; in them it seems clear that the blood-stream is infected at an earlier date than the meninges. Experimental blood inoculations in animals have completely failed to produce meningitis, just as intranasal inoculations have failed. It seems clear that the question of the mode of entry of the meningococcus into the meninges must await further experimental work for its answer.

§ 3. **Stages in the Process of Meningococcus Infection.**—This is perhaps the most convenient place in which to refer to a conception of the disease originally put forward by Dopter and recently revived in this country by Lundie, Thomas, Fleming, and Maclagan as the result of their observations in the Aldershot command in the spring of this year. These authors consider cerebro-spinal fever as a disease having three stages—an initial stage of naso-pharyngeal catarrh, a second stage of septicæmia, and a final meningitic stage. The catarrhal stage is thought to be very prevalent, but to give rise to few or no symptoms. The septicæmic stage is common, but its existence goes very largely unrecognized; it is most often mistaken for influenza. The meningitic stage is 'terminal' and only occurs in a small percentage of the cases of infection. This view, needless to say, comprises the whole series of possible pathogenic events open to the meningococcus, rather than connotes the disease-process to which it most often gives rise. Considered epidemiologically, and from the point of view of preventive medicine, the idea is useful, because it draws attention to the naso-pharynx as the habitat of the meningococcus, and encourages efforts at checking the diffusion of the micro-organism. But it does not harmonize with clinical facts nor, so far as these are available, with pathological data. In most of the carriers there are no evidences of inflammation of the naso-pharynx that can reasonably be attributed to the presence of the meningococcus.[1] The 'septicæmic stage' of cerebro-spinal fever, *prior to the development of meningeal symptoms,* fails of proof; positive blood-cultures after the invasion of the meninges has taken place may reasonably be set down to the escape of the meningococcus into the circulation from the pia-arachnoid space, as is known to occur in the case of monkeys which have received intrathecal injections of the coccus. Lastly, this conception of the disease takes little account of the fact, for which there is such overwhelming evidence, that *the pia-arachnoid tissues are pre-eminently the seat of election of the meningococcus in all individuals for whom it is pathogenic.* To relegate what is certainly the most specific lesion caused by the meningococcus to the category of a terminal or accidental effect is equivalent to considering the consolidation of the lung in pneumonia as of less importance than the presence of the pneumococcus in the upper respiratory tract and in the blood-stream, important facts though both of these may be.

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[1] The soldier's pharynx is rarely free from some degree of congestion, catarrh or œdema. To neglect other possible ætiological factors than the operation of the meningococcus when considering this question would be an obvious fallacy.

In those districts in which pneumonia is epidemic, as in New York, it is doubtless very important to make exact determinations of, and to draw special attention to, the degree of incidence of the pneumococcus in the upper respiratory tract, and, as already remarked, the epidemiologist may be permitted to enlarge upon the constancy with which the meningococcus is found in the naso-pharynx. Arkwright, re-stating Dopter's doctrine, sums up the position very clearly as follows :

'The large number and widespread distribution of carriers and the small number of cases of meningitis compared to the population forces upon one the view that for a true understanding of an epidemic of meningitis the total number of persons who harbour the meningococcus should be looked upon as constituting the true epidemic. Some of these persons are not ill in the ordinary sense of the word, though they are attacked by the meningococcus and successfully attacked in different degrees: First, according to the amount of change produced in the nasal and pharyngeal mucous membrane (this may be considered the first stage of the disease); secondly, according to whether the meningococcus succeeds in infecting the blood, meninges, joints, &c. From this point of view —the epidemiological one—the carriers constitute the mass of the epidemic, and those who subsequently develop meningitis are only a small accidental minority.' (*Brit. Med. Journ.*, March 20, 1915.)

§ 4. **Mode of Production of the Symptoms of the Disease.**[1]—The symptoms of cerebro-spinal fever fall readily into three groups: (i) the fever with its customary associations seen in all acute infections; (ii) the symptoms directly attributable to the specific coccus circulating in the blood and its local action upon certain organs and tissues; and (iii) the nervous symptoms. The first two categories do not call for any comment.

The nervous symptoms are attributable to one or more of three morbid changes induced by the disease:

(i) Increased tension of the cerebro-spinal fluid, as the result of hypersecretion from the choroid plexuses, blocking of the usual channels of elimination of the fluid, and the transudation of blood serum into the pia-arachnoid space.

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[1] In this section the writer follows the views of Netter and Debré.

(ii) Changes in the circulation of the central nervous system, due to actual lesions in the small vessels and to vaso-motor influences.

(iii) The meningitic inflammation produced by the toxic action of the meningococcus upon the brain, cord, and nerve roots.

The headache is probably due to more than one of these conditions. The most important cause is probably the hypertension of the cerebro-spinal fluid, because the pain is often considerably relieved by lumbar puncture. Other possible factors are the irritation of the sensory nerves of the meninges, and the changes in the cerebral circulation.

The pains and hyperæsthesiæ are probably due to the irritation of the posterior nerve-roots. But here, again, the tension of the cerebro-spinal fluid is also a factor, since its evacuation relieves the pains and injection of serum increases them.

The rigidities are more difficult to explain. They may be due to irritation of the posterior nerve-roots, or to irritation of the anterior horn-cells and the corresponding cells in the bulb. Increased tension of the cerebro-spinal fluid does not appear to enter into their production.

Vaso-motor changes, alterations in pulse, and polyuria are probably due to irritation of the floor of the fourth ventricle, the ependymal lining of which shows marked changes, often visible post mortem to the naked eye.

The herpes shows affinities with true herpes zoster, and may reasonably be attributed to the changes in the posterior root ganglia which have been demonstrated post mortem.

The muscular wasting which is such a marked feature of the disease, especially in its protracted forms, is to be referred to the loss of proper trophic influences from the damaged anterior horn-cells and anterior nerve-roots. The loss of the tendon reflexes, when this occurs, is to be assigned to the same cause.

Paralyses own more than one factor in their causation. Temporary mono- and hemiplegias are due to transient difficulties in the cerebral circulation, with œdema of the underlying tissue. More persistent instances of hemiplegia, however, must be referred to definite lesions in the cerebral cortex, such as thrombosis, hæmorrhage, or acute encephalitis. Paralyses of the limbs or cranial nerves are more likely to be due to changes in the nerve-roots.

CHAPTER XI

MORBID ANATOMY AND HISTOLOGY

The pathological appearances found post mortem in patients dead of cerebro-spinal fever are almost confined to the central nervous system and its membranes, upon which the brunt of the meningococcus infection almost invariably falls. In this chapter a brief description will be given, in this order, of the naked-eye appearances of the brain and spinal cord, of the microscopic changes in these organs, and of certain changes found elsewhere in the body.

I. Naked-Eye Appearances in the Brain and Spinal Cord

§ 1. **General.**—There are no appearances in the brain and cord that are in any way characteristic of meningococcus infection as against infection by other pyogenic micro-organisms such as the pneumococcus or streptococcus pyogenes. Both the character of the exudate and its distribution in a fatal case of pneumococcus meningitis may closely simulate those of meningococcus meningitis; the nature of the infection must be judged entirely by the bacteriological evidence.

The appearances in a fatal case of cerebro-spinal fever vary with the severity and with the duration of the disease. Three main types of morbid appearances are met with in the post-mortem room, according as death has occurred very early in the disease, during the acute stage or during the chronic stage.

§ 2. **Appearances in a Fulminating Case.**—On removing the skull-cap the dura is seen to be tense, and its vessels full. Small hæmorrhages may be present in it. When this membrane is opened fluid escapes, not in large amount and not purulent. The surface of the arachnoid, adherent to the dura, is noticed to have lost its lustre. The brain appears larger than normal and is, in fact, swollen. The convolutions are flattened and the sulci shallow—changes due partly to the softening effect of the acute inflammation and partly to the pressure of the increased fluid in the ventricles. Both of these last-named changes are more apparent in the brains of infants, as also is the alteration in general shape of the organ whilst lying on the table: in acute meningitis the brain tends to spread out on its base, so that, by comparison with the healthy viscus, it loses much of its characteristic shape. The pial vessels are seen to be full of blood, and many more vessels can, on this account, be seen than in health. The result of the congestion is to produce a salmon-pink hue in the organ, another marked contrast with a normal brain placed alongside it. On closer examination it is found that the convolutions are somewhat softer to feel than in health. A little turbid fluid lies along the sulci, and is collected in the cisternæ. The ventricles are slightly distended by similar fluid. There is nowhere any purulent exudate.

§ 3. **Appearances in a Case of the Ordinary Type.** —When the infection has been less fulminating in character, but still very acute, and when death occurs some time after the third or fourth day, but before the chronic stage of the disease has developed, the appearances are as follows: Little or no fluid escapes on opening the dura. The surface of the brain, though injected, is less generally pink than in the fulminating case. The feature attracting chief attention is the purulent exudate, which has, in most cases, some such character and distribution as is here described. It is very thick, yellowish-green in colour, and sticky in consistence. It is disposed chiefly at the base of the brain, with a special accumulation about the bulb. In the post-basic infection of infants, when death occurs early, this accumulation of pus is the chief one found. Flattened extensions of it run up the various sulci towards the vertex, which, though not escaping altogether, is often relatively free from involvement. These extensions of pus are seen to follow the vessels from the base. In a number of cases a curious concentration of the purulent exudate is seen to cap the tips of the frontal lobes, and often to spread a little on to the convexity of this part of the brain. The optic chiasma and the perforate spaces, anterior and posterior, are usually bathed in pus, but the olfactory nerves generally escape. The crura cerebri and the upper surface of the cerebellum are often the seat of another collection.

The ventricles are moderately dilated, the fluid in them being usually slightly turbid with flakes of fibrinous material,—not pus of uniform consistency. The ependymal lining is pinkish and rough.

§ 4. **Appearances in a Chronic Case.**—There is usually an escape of a good deal of thin turbid fluid when the dura is opened. The surface of the brain shows little or no purulent exudate. Instead, there are local thickenings of the pia-mater, and also of the arachnoid ; these membranes are often adherent to each other and to the underlying brain tissue. Loculi of turbid fluid are present. Some of the more dense thickenings are yellowish in colour, especially about the body of the sphenoid and the region of the bulb. This part may need careful dissection in order to get it away intact. The convolutions are pale, not pink, and are much flattened. The brain as a whole flops on the table, its convexity falling flat as a result of the dilated ventricles and the thinning of their roof.

The ventricles are full of thin turbid fluid with large flocculi in the horns, themselves very conspicuous structures owing to enlargement. The ependyma is irregularly thickened and absorbed.

If the infection has entirely subsided, and death has occurred as a result of emaciation and chronic hydrocephalus, there may be very little to see on the surface of the brain, a few local thickenings and adhesions of the membranes being the sole representatives of the original meningitic inflammation.

§ 5. **Appearances in the Spinal Cord.**—Routine examination of the cord shows changes very similar to those in the brain at the different stages of the disease. In the fully developed stage of infection the exudate is found chiefly upon the posterior aspect of the cord, and there is most often a special concentration of it about the lumbar enlargement. To a less extent a similar concentration occurs in the cervical region.

II. MICROSCOPIC APPEARANCES

§ 6. **Situation of Earliest Changes.**—There is some doubt as to the exact histological point at which the inflammation begins in meningococcus meningitis. But it is probably in the arachnoid mater. Westenhoeffer described early changes in and near the vessels of this membrane at a time when the pia-mater at the depths of the sulci—where the arachnoid mater does not follow it—was free from morbid appearances. Most authorities agree that the early changes are synchronous in the brain and in the cord. If this be so, it is an important fact in support of the view that the route of entry of the coccus into the membranes is by the blood-stream, rather than locally by the lymphatics and solid tissues from the naso-pharynx to the region of the bulb.

§ 7. **Nature of Earliest Changes.**—These consist of congestion of the small vessels of the membranes with leucocytic infiltration of their walls and of the neighbouring tissue spaces. Multiple venous thromboses take place. A serous and fibrinous exudate appears, and later the formation of pus. Throughout the process the leucocyte is the dominant cell found by differential staining. The lymphocyte is less concerned. There are many very large tissue cells present in the inflammatory area, phagocytic for smaller cells, and thought to arise from the connective tissue of the membranes or from the adventitial coat of the small vessels.

§ 8. **Later Changes.**—As the changes proceed a purulent infiltration of the pia-arachnoid spaces takes place, with those accumulations of the exudate that have been already described.

The *grey matter* immediately underlying the pia-mater invariably suffers, as it does in all forms of acute leptomeningitis.[1] The vessels are dilated and a perivascular infiltration occurs. The brain tissue becomes slightly œdematous.

The *ventricular walls* are inflamed and œdematous, and similar changes may be demonstrated here as in the superficial layer of the cerebral cortex.

Certain *degenerative changes in the parenchyma* of the central nervous system have been demonstrated in long-standing cases, but they do not form a characteristic feature of the morbid process.

§ 9. **The Demonstration of the Meningococcus** in the infiltrated areas, and in the free exudate, originally described by Weichselbaum, has since been confirmed by all responsible workers. It is, indeed, only in very malignant cases—where death occurs more as the result of the septicæmia than the changes in the brain—and in very chronic cases, such as some of the protracted post-basic cases, that any difficulty is found in this demonstration. It may be said truly that the occurrence of the meningococcus in association with the specific morbid tissue changes of cerebrospinal fever is at least as constant as is the occurrence of any micro-organism in association with the changes found in any other disease for which this micro-organism is regarded as being the *materies morbi*.

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[1] Strictly speaking, all cases of leptomeningitis are, pathologically considered, cases of meningo-encephalitis. This conception renders clearer some of the clinical features of the disease-process.

§ 10. **Appearances in other Organs.**—(i) *The blood.* The meningococcus can often be grown from the heart's blood in patients dying during the first week of infection.

(ii) *The naso-pharynx and nasal sinuses.* Although this is the site of entry of the meningococcus into the body, there are no special changes found post mortem. Hyperæmia and increased secretion are present, but so they are in most acute infections. Pus may be present in the sphenoidal sinus, and, less frequently, in the other accessory sinuses of the nose. The meningococcus can usually be recovered from the naso-pharynx during the first fortnight of the disease.

(iii) *The lungs.* The changes of bronchial catarrh can often be demonstrated in cases dying early in the course of the disease, and especially in infants and young children. In some epidemics there is a special tendency to consolidation of the lung, both lobular and lobar. The meningococcus is occasionally recovered from the exudate in these cases, but the pneumococcus more frequently.

(iv) *Intestinal tract.* If the case has been very acute, changes are usually present, and may be very conspicuous. They consist of small hæmorrhages and swelling of the Peyer's patches and other lymphoid collections. There is, however, nothing specific about these changes, and they do not give much support to the view that the intestine may be a portal of entry for the meningococcus.

The other organs of the body show only occasional changes. It is one of the features of the disease that the brunt of the toxic action of the coccus falls upon the cerebral membranes almost entirely. Reference should, however, be made to the state of emaciation of the body in a great number of the cases which arrive at the post-mortem room ; in all except those in which death occurs during the first fortnight this emaciation is conspicuous.

CHAPTER XII

PROGNOSIS

§ 1. **Mortality of the Disease; Effect of Serum Treatment.**—The mortality in cerebro-spinal fever is undoubtedly higher in the epidemic than in the sporadic cases, if the post-basic meningitis of infants, in which the mortality is very high, be excluded. There are, however, no good figures upon which to base an estimate of mortality in the sporadic cases. In epidemics the mortality prior to the introduction of serum treatment was about 70 to 80 per cent. Since the serum treatment the mortality in epidemics has fallen to 30 to 40 per cent.[1]

§ 2. **Effect of the Stage of the Epidemic upon Mortality.**—It is generally agreed that the mortality is higher in the early stages of an epidemic than towards the fall of the curve of incidence of the cases. This corresponds with the general experience that there is a larger proportion of fulminating and very severe cases during the evolution of an epidemic and a larger proportion of mild and abortive cases when the epidemic is on the wane.

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[1] In Flexner's analysis of 1,300 cases at the Rockfeller Institute the mortality among the cases treated by serum was 30·9 per cent, as against 70 per cent among cases not so treated. Robb, in the Belfast epidemic, found a mortality of 30 per cent in serum-treated cases, and 72·3 per cent in others. Dopter's statistics yield 16·4 per cent and 65 per cent for the two groups respectively. Other observers give figures more or less similar to Flexner's.

§ 3. **Influence of Age.**—This is noteworthy. The disease is extraordinarily fatal in infants (patients under 2 years of age). This statement holds good both for the post-basic cases, which are so often subacute or chronic in character, and for the acute cases. The mortality is lowest between the ages of 5 and 10 years.

§ 4. **Symptoms unfavourable to Prognosis.**—A fulminating form of onset is invariably bad, and the mortality in these cases is very high, if indeed it is not 100 per cent. In the cases with less vicious invasion symptoms, one or more of the following symptoms betoken a grave issue : early loss of consciousness, wild delirium, persistent insomnia, extensive hæmorrhagic eruption, cyanosis. Later in the course of the disease the worst sign is the appearance of hydrocephalus.

§ 5. **Symptoms that are equivocal in respect of Prognosis.**—The degree of fever, the intensity of the headache, the amount of rigidity, the presence of marked emaciation, frequency and irregularity of the pulse, rhythmical respirations, the presence of herpes —none of these things yields any information of value in predicting the issue of the disease. *In few other diseases, if in any, is it possible for the patient to be so ill and yet to recover completely, as in cerebro-spinal fever.*

§ 6. **The State of the Cerebro-spinal Fluid in relation to Prognosis.**—This, it is important to remember, is also to a high degree equivocal. (See Chap. IV, § 5.) No reliance must be placed upon it except for purposes of diagnosis. It may be almost clear and may contain very few meningococci, and yet the patient may be desperately ill and like to die. On the contrary, it may be highly purulent and crowded with meningococci, and yet the patient may get rapidly well. There is, however, one point in the examination of the exudate which bears upon prognosis, and that is the extent to which the cocci present are intracellular. The more marked this is, the better the outlook, and vice versa.

§ 7. **The Effect of Early Serum Treatment.**—As Netter and Debré point out truly, *the most important fact bearing upon prognosis is the stage in the disease at which serum treatment is begun.* Flexner found that if serum was given between the first and third days the mortality of the disease was reduced to 18·1 per cent; if it was delayed until the seventh day the mortality rose to 36·5 per cent.

CHAPTER XIII

TREATMENT

§ 1. **Specific Nature of the Treatment.**—Cerebrospinal fever is not only a specific disease in regard to its ætiology, it is specific also in regard to its therapeutics. Given that treatment by anti-meningococcus serum is early and thorough, the disease is curable in the large majority of cases.

It is of vital importance that the first dose of serum be given at the earliest possible moment after the disease is diagnosed or is strongly suspected. Nothing in the treatment of the patient should take precedence of this first serum administration. This chapter begins, therefore, with an account of the administration of the serum. It should be read in connexion with Chapter V, dealing with lumbar puncture.

There are several immune sera on the market; the serum most in vogue in Great Britain and in America is prepared after the manner of Flexner, and goes by his name. If the result of using one brand of serum in a particular case is unsatisfactory, a different brand should be tried, and even a third, if necessary. It may even be advisable to prepare a special serum for the cases of a particular epidemic (see Chaps. III and XIII).

The serum must be given by the intraspinal route; it has probably no therapeutic value in the ordinary type of case if given subcutaneously or intravenously. The intravenous route should, however, be chosen in the treatment of meningococcus septicæmia. And a dose of 20 c.c. of serum may be given subcutaneously, to supplement the intraspinal dose, in all very acute and severe cases.

§ 2. **Methods of Intraspinal Administration of Serum ; Dosage.**—The serum may be allowed to flow into the spinal theca by gravity, or it may be injected by means of a serum syringe. The rapid injection of serum is harmful and may even lead to a fatal result ; but it is doubtful if the injection method is prejudicial provided due care be exercised. The amount of pain caused by the use of the syringe, however careful the operator may be to avoid sudden pressure on the piston, is usually greater than when the serum is allowed to flow in by gravity. The writer has used both methods and recommends the gravity method by preference, although it must be confessed that the recommendation is based chiefly upon a consideration of general principles rather than upon experience of results.

In England it is not customary to rely upon any pressure measurements as a guide to the amount of serum used or to the rate at which the flow should take place. The amount of serum is chosen arbitrarily and the rate of flow is made as slow as possible consistent with completing the procedure in a reasonable time. In infants 5–10 c.c. is the usual dose ; in children 10–20 c.c. ; in adults 25–40. The introduction of the serum should last at least 10 minutes, whichever of the two methods is chosen. There is probably nothing to be gained by extending the operation over a longer period than 20 minutes.

In America Sophian has strongly recommended the control of the serum administration by concurrent observations of the blood-pressure by an assistant. This author finds that in the great majority of cases there is a fall of blood-pressure with the withdrawal of cerebro-spinal fluid, and that this fall is continued with the introduction of the serum. Sophian recommends that the withdrawal of fluid should cease if the blood-pressure falls by 5 mm. in a child or by 10 mm. in an adult. If there is no such fall of blood-pressure with the withdrawal of fluid this is allowed to flow until the pressure of the cerebro-spinal fluid is normal, which may be judged to be the case when the fluid drops once every 3–5 seconds. When the introduction of the serum has caused a further material fall of blood-pressure it is thought advisable to stop, even if there are no other clinical indications for so doing. Sophian gives no figures to act as a guide in this matter, but it is to be inferred from reading the account of his method that a second fall of 5 mm. in a child, or of 10 mm. in an adult, should be taken as an indication for stopping the serum administration.

§ 3. **Preparations for the Serum Administration.**—Whether given by gravity or by the syringe, the serum should be warmed to body-heat before use, by placing the phial containing it in a basin of hot water. This is done before the lumbar puncture is performed.

The necessary apparatus for introducing the serum is also sterilized and got ready prior to the lumbar puncture. There need be little fear about removing too much fluid by the lumbar puncture. It is of great importance, however, to avoid any attempt at introducing a larger bulk of serum than the amount of fluid evacuated. When the amount of cerebro-spinal fluid decided upon is withdrawn the stylet is replaced in the needle, which is left *in situ* pending the preparation of the serum and of the patient's position. These things are attended to by the assistant, because the operator is engaged in steadying the needle and in ensuring that it is kept in position. The patient's hips are raised on to a firm bolster or cushion; the shoulders are already low in the bed (see Chap. V, § 4). The foot of the bed is raised at least a foot by blocks or by large books that have been got ready beforehand. It is usually recommended to put the patient in this semi-inverted position *after* the serum is introduced, but the writer considers it even better to do so whilst the serum is running in. The tendency to distension of the lumbar cisterna by the serum is thereby diminished, and the diffusion of the heavier serum with the lighter cerebro-spinal fluid in the narrow thecal sac around the thoracic cord, and thence with the fluid of the cerebral cisternæ, is assisted from the first.

§ 4. **Introduction of the Serum by Gravity.**—The apparatus used is extremely simple; it consists of two feet of rubber tubing, with a cylindrical glass funnel at one end and a bull-dog clip near to the other end; the rubber tubing is of such a bore that it fits accurately over the end of the lumbar puncture needle. The needle of the apparatus, or a duplicate needle, has already been used for the lumbar puncture. The rubber tube and the glass funnel have been sterilized by boiling and are lying ready for use in hot water. Some of the American serum is supplied in glass tubes, which can be used as funnels by attaching them directly to the rubber tube. If the serum is supplied in a phial with a narrow neck it must be transferred to the funnel. The rubber tube, filled, of course, with the serum, is now attached to the needle, and the funnel is held at such a height above the patient that a slow but steady flow is kept up. The temperature of the serum is prevented from falling unduly by the assistant grasping the funnel in the hand by which he holds it. With a tube 18 inches long the flow will not be too fast if the funnel is held at full height. If the tube is longer than 18 inches there is considerable waste of serum in filling it; for although, in theory, the serum in the tube should run into the spinal canal and its progress be noted by means of the small glass inset placed for the purpose, in practice this seldom happens, and the operator is fortunate if the flow proceeds normally as far as the bottom of the funnel. And yet, despite the more tedious nature of the process, the gravity method is to be preferred.

§ 5. **Introduction of the Serum by Syringe.**—If this method is chosen, either because the operator is single handed or because he has not got by him the necessary apparatus for the gravity method, it is preferable to make use of the small rubber junction usually supplied with the serum syringe rather than to connect the nozzle of the syringe directly with the end of the lumbar puncture needle. By so doing, slight movements on the part of the patient do not interfere with the introduction of the serum by changing the position of the needle; nor is the pressure exerted on the piston transferred quite so directly to the pia-arachnoid space. The greatest care must be exercised to equalize as far as possible the pressure on the piston. The whole procedure should be done in leisurely fashion; at least one minute should be allowed for each c.c. of serum injected. It will be found that a rotatory movement of the piston is of help in avoiding jerkiness in advancing it along the barrel of the syringe. It goes without saying that the piston must work quite smoothly in the barrel; hence an all-glass syringe is a desideratum. If a syringe is used of smaller capacity than the amount of serum employed the syringe must be detached from the needle and refilled, the stylet being replaced in the needle during the process. The phial of serum should be kept warm meanwhile.

The serum having been introduced by one of these methods, the needle is promptly withdrawn by the right hand, the skin being supported by firm pressure of the left index-finger placed close to the needle. The puncture wound is sealed by a little gauze or wool soaked in collodion.

The semi-inverted position of the patient is maintained for a full hour after the serum has been administered.

§ 6. **Immediate Ill-effects of Serum Administration and their Treatment.**—*Pain* is common and may be severe. It is usually referred to the back and legs, less often to the abdomen. If the serum is injected by a syringe, exacerbations of pain often occur with each push of the piston, however gentle this may be. So definite is this that it is difficult to avoid the conclusion that the pain is due to local distension of the spinal theca at the level of injection. If the serum is not properly warmed the pain is aggravated. Sophian has suggested the ingenious expedient of what he terms ‘ water anæsthesia ’; the patient is encouraged to sip water through a straw during the operation. This device appears to render the pain more tolerable and to lessen the patient's restlessness. If the pain persists after the operation is over, the local application of a large hot fomentation often gives relief.

Symptoms of *collapse* may occur, but are not commonly seen if the operation is carefully performed. The condition of the patient is, of course, carefully watched during the introduction of the serum, and for several minutes afterwards. If, during the operation, the mental state changes for the worse—the stupor increasing—if the respirations become irregular, or the pupils dilate, or the pulse alters in any respect unless it be for the better, or the rigidities pass off, the patient becoming flaccid, it is wise to desist from further introduction of serum. It is doubtful to what pathological condition these alarming, but fortunately uncommon, symptoms are due. Netter and Debré think they may be due to a sudden œdema of the nerve tissues, analogous to the œdema which sometimes follows the subcutaneous injection of serum (Arthus' phenomenon). Others think these symptoms are due to increased intraspinal pressure. Carter's experiments on dogs led him to conclude that cardiac inhibition and respiratory depression were the results of increased intraspinal pressure. This observer recommends atropine and cocaine, given hypodermically, for the purpose of counteracting these ill effects. If the breathing becomes bad, or ceases, artificial respiration must at once be resorted to.

The *temperature* not infrequently rises suddenly after serum administration and the thermometer should invariably be used after the procedure. A temperature of 103° or more should be met by immediate sponging or by cradling (see Chap. VII, § 6).

§ 7. **General Management of the Patient after the first Serum Administration.**—The *room* chosen for the patient should be as large and airy and quiet as the house can provide. All unnecessary furniture should be removed. The blinds should be drawn, and only raised when observations are being made or when lumbar puncture is being performed.

The *nurse* should be carefully chosen, and should by preference be one with experience of this disease or of 'acute head cases'. She must have received training in the care of the mouth and secretions, in the management of the skin, and in methods of special feeding. She must be warned to be scrupulously careful of her own person and must understand the importance of strict asepsis.

The *posture* of the patient will be largely determined by the severity of the disease-process. He may be allowed to lie in his position of greatest comfort (see Chap. VII, § 1) for long periods of time. At intervals, however, he should be carefully turned. The head and shoulders should be kept somewhat raised at all other times than those when serum has just been administered.

The *diet* is to be adjusted to the patient's condition. The disease is an exhausting one, and as full a dietary as is consistent with the state of the digestive secretions is to be allowed. There is therefore no contra-indication to semi-solid food, such as bread-and-milk, custards, and minced under-cooked beef and mutton, in patients who are fully conscious, whose tongues are moist, and whose abdomens are free from flatulence. If the fever is a conspicuous feature and the patient is drowsy or delirious, the mouth is usually dry ; the diet is then necessarily restricted to fluids, which should be given in the form of diluted milk, and freshly prepared meat essences, in small quantities at frequent intervals. Water should be given freely. If the patient is in a state of stupor the act of swallowing must not be relied upon ; feeding must then be by the passage of a nasal tube three or four times in the twenty-four hours. According to the age of the patient, from five to ten ounces of citrated milk and water (equal parts), or of peptonized milk, or of beef essence, are allowed to run into the stomach from a funnel attached to the tube and held at the necessary height above the bed. A raw egg may be beaten up in the milk and a little brandy may be added if the state of the heart indicates the use of alcohol. If *vomiting* is troublesome, peptonized milk only should be used, or whey or albumin water. If this symptom is persistent it may be advisable to put no food at all into the stomach for 24–48 hours, relying upon saline injections (5–20 ounces according to age) *per rectum* every six hours, supplementing these, if thought desirable, by the subcutaneous use of a 10 per cent. solution of dextrose in normal saline.

The bowels are usually constipated ; it is therefore frequently necessary to use purgatives : castor oil or calomel followed by a saline, or compound liquorice powder. If the patient is comatose early in the disease, when treatment is beginning, it may be advisable to give two minims of croton oil in butter or moist sugar.

Urinary difficulties do not usually occur unless the patient is unconscious, in which case it is important to bear in mind the possibility of retention, which may lead to 'overflow incontinence'. This condition indicates the use of the catheter, with the customary care in the matter of asepsis.

§ 8. **Is any Drug of Service in checking the Disease-process ?**—It is exceedingly doubtful if any drug exercises a beneficial influence upon the infection.

Since it was shown by Cushing and Crowe that *urotropin* was secreted into the cerebro-spinal fluid when given by mouth, this drug has frequently been prescribed in all forms of meningitis. Sophian recommends it for prophylactic use in cerebro-spinal fever. The idea that urotropin might 'disinfect' the cerebro-spinal fluid derived some support from Flexner's finding that the administration of the drug to monkeys prior to infecting them with the virus of poliomyelitis conferred some degree of immunity upon the animals. It is not possible to say if the course of cerebro-spinal meningitis is much altered by its use.

Soamin (sodium aminophenylarsenate) has recently been advocated as possessing the power of controlling the meningococcus infection. According to George Low, who has summarized our knowledge of this treatment, soamin was originally used by Arnold Johnston in two cases of cerebro-spinal fever in 1910. The drug was largely used by R.A.M.C. officers in Africa, following their experience of it in the treatment of sleeping sickness and of syphilis. Shircore and Ross treated 127 patients by means of soamin out of an epidemic of 143 cases occurring in British East Africa in 1913. Thirty-seven of these cases were of the 'malignant' kind, dying within 60 hours of their coming under observation. Excluding these 37 cases the mortality in the 90 remaining cases was 37·78 per cent. These observers were even led to give up serum treatment in favour of soamin. But the failure of the particular serum used in this epidemic may have been due to its possessing too low a potency. Arnold Johnston administered the drug intravenously. In the African cases it appears to have been given intramuscularly. Gilks, who also used soamin in East Africa, gave 5 grains in aqueous solution intramuscularly on each of the first two days of the treatment, and followed these two initial doses by 3 grains on the fourth day. If the disease failed to show definite signs of subsidence after these doses, occasional further doses were given. The question arises whether, as suggested by Batten, if it is decided to try the effect of an arsenical preparation, it would not be better to use neo-salvarsan or salvarsan intravenously. By these means there would be obviated the risk, slight though it may be with the small doses of the drug used by the above-named workers, of producing optic atrophy, a known possible consequence of soamin administration. It is difficult to realize that any preparation of arsenic can influence a meningitis once this has arisen, seeing that such substances do not appear to pass the barrier of the choroid plexus and reach the cerebro-spinal fluid. It does not seem so unlikely, however, that such preparations, if given during the 'septicæmic' stage of the disease, may inhibit the activity of the meningococcus. But it will be readily allowed that in this, as in all therapeutic questions, the ultimate proof of efficacy lies in the practical experience of the remedy; and the results above recorded are certainly sufficiently striking to warrant careful consideration. The writer has had no personal experience of these arsenical preparations.

Iodides and *mercury* are not infrequently exhibited. These drugs probably receive their support from the analogy of their use in cases of cerebral syphilis particularly, and in cases of acute inflammations generally. It is the writer's custom to prescribe the following mixture in most cases of cerebro-spinal fever, the size of dose being chosen according to the age of the patient :

℞.
Liq. hydrarg. perchlor. ♏ xx–ʒ j.
Potass. iodidi gr. iij–x.
Ext. glycyrrhiz. liq. ♏ x.
Aquam dest. ad ʒ ss.–℥ j.
S. Sextis horis.

The desire of the practitioner not to deny the patient any possible assistance seems to be the most powerful argument for the use of any of these remedies.

§ 9. **The Treatment of certain Symptoms.**—*Headache* is usually the most distressing symptom calling for special treatment. In all but the mildest cases of the disease it is a good thing to shave the scalp and to apply an icebag or Leiter's tubes. A leech over each mastoid is sometimes followed by relief for several hours. If, as is often the case, the pain is referred to one particular spot, the leech should be applied there. Drugs are not of much use in controlling the very severe headaches, but antipyrin, caffein, and aspirin may all be tried in full doses. Morphia may be imperative in some cases, because nothing else may be of any service.

Restlessness, delirium, and *insomnia.* If these symptoms are troublesome a trial should be given to some such combination as the following :

℞.
Ammon. bromid. gr. x–xxx.
Tr. valerian. ammon. ♏ x–xxx.
Syr. chloralis ♏ xx–ʒij.
Aquam dest. ad ℥ss.–℥j.
S. Secundis horis ad doses iv–vi.

The *pains* and the *stiffness* are best treated by warm baths, at a temperature of 102°–104° F. French physicians use these baths a great deal. If employed they should be given for half an hour three or four times in the twenty-four hours.

If the delirium is exhausting or the condition verges upon mania, vapour of chloroform may be used, or morphia with atropine maybe given. Hyoscine should be avoided.

Cachexia. The progressive emaciation which sets in where the disease takes on a chronic course, with or without hydrocephalus, should be met by constant efforts at supporting nutrition by special feeding, by tonics, and, if indicated, by saline and dextrose infusions.

Arthritis. The affected joint is best treated by fixation, by the application of hot stupes, and by aspirin internally. If the fluid effusion becomes considerable, or does not quickly yield to these measures, the joint should be aspirated and 5–10 c.c. of serum should be injected into it if the meningococcus is demonstrated in the fluid.

§ 10. **The Repetition of the Serum Administration; Indications.**—Flexner laid down an arbitrary rule for guidance on this matter, recommending the use of serum daily for four or five doses and advising that after this the practitioner should be influenced by the subsequent clinical condition of the patient and by the state of the lumbar puncture fluid at successive operations. Some such custom as this remains the usual one in the *ordinary type* of the disease. It is desirable to vary this rule in individual cases.

If the case is of the *superacute type* it is well to repeat the dose of serum in eight to twelve hours and again after the same interval. In this way an effort is made, consistent with the precautions already referred to, to get as much serum as possible into the cerebro-spinal sac during the early stages of the disease. After these initial three doses an interval of twenty-four hours may be allowed to pass before the next dose is given.

If the case is a *mild* one the original serum administration needs not to be repeated for twenty-four hours, and the second interval may be forty-eight hours provided the course of the disease is satisfactory. Although in very mild cases one administration of serum with the drainage it entails is often sufficient to establish definite and lasting improvement, this must never be depended upon, as sudden 'relapses' are common in the disease and are certainly preventible by adequate use of serum.

No doubt the best indication for the repetition of the serum is the condition of the meningitic exudate as seen at successive punctures. The lumbar puncture fluid should always be examined by a competent observer whenever this is possible. The indication for further serum is proportionate to the number of meningococci still present in the extracellular form. But it is not often practicable to prepare a stained film of the fluid straightway so as to be guided by the result. The decision whether to use serum or not must in most cases be determined by a consideration of the clinical condition together with the naked-eye characters of the fluid. In regard to the latter it may be said that if the fluid is still turbid (indicating the presence of polymorphous cells) it is well to give more serum. If serum is not given upon the occasion of any puncture, and the pathologist reports extracellular cocci in the specimen examined from that particular puncture, this should decide the practitioner to give serum at the puncture next undertaken, whatever the naked-eye features of the fluid may be.

§ 11. **Relapses** must be at once met by a further series of doses of serum, given in precisely the same manner as at first. There appears to be no arbitrary limit to the amount of serum which it is advisable to give. Netter and Debré quote a case which recovered after twenty-five injections, during which no less than 800 c.c. were given.

§ 12. **The Repetition of the Lumbar Puncture.**—A lumbar puncture of necessity precedes each intraspinal dose of serum. But there arises in many cases an indication for continuing the lumbar punctures over a longer period than that covered by the serum administrations. Any further untoward event in the course of the disease, or any undue prolongation of it, is best met by repeating the puncture. The amount of fluid withdrawn is determined by the amount present, and its characters. Too much is not likely to be withdrawn. If the temperature rises after having settled for two or three or more days; if there is an exacerbation or a recurrence of the headache, restlessness, delirium, or insomnia; if rigidity returns after an initial subsidence—in either of these instances it is advisable to investigate the pressure and the characters of the cerebro-spinal fluid. There are reasons for thinking that further drainage at certain intervals tends to prevent the development of the most serious of the complications of the disease, a state of hydrocephalus. It may therefore be necessary to repeat the puncture several times, especially in the more chronic cases and in the group of post-basic cases in infants.

§ 13. **Puncture of the Ventricles in Hydrocephalus; Intracerebral Injection of Serum.**—If a condition of hydrocephalus has been diagnosed, it is advisable to tap the lateral ventricles and to inject serum. This procedure is not so difficult nor so dangerous as may be supposed.

(i) The patient is usually an *infant*, with open fontanelles. The region of the anterior fontanelle is shaved and the skin is sterilized. A stout needle, to which a syringe can be attached, is inserted at the lateral angle of the fontanelle, and is gently pushed towards the mesial line for a distance of an inch or an inch and a half. The fluid is usually under considerable pressure, so that it becomes quickly known when the needle reaches it. It is not necessary or advisable to attempt to withdraw more fluid than comes into the syringe with very gentle aspiration. With great care, an amount of serum less in bulk than the fluid withdrawn is now introduced into the ventricle.

(ii) In *older children* and *adults* the operation of decompression becomes necessary; and here again, though a much more serious procedure, the practitioner should not hesitate to give the patient the benefit of the operation and of the use of serum by this special route.

§ 14. **Treatment by Meningococcus Vaccine.**—The effects of inoculation treatment in cerebro-spinal fever have hitherto been very variable, and there is no evidence for thinking that such treatment can compare with treatment by serum in respect of beneficial results. To what degree it is advisable to use meningococcus vaccine as an adjunct to serum treatment is at present quite a speculative consideration; and the choice of the time to begin and the doses to give are equally matters of individual opinion. That specific effects are actually produced by the vaccine in certain cases is clearly proved; the difficulty lies in our lack of exact knowledge on the above-mentioned points of practice. Chart 8 illustrates the good effect of an autogenous vaccine used during the later part of the disease, at a time when recovery was delayed and the patient threatened with chronic

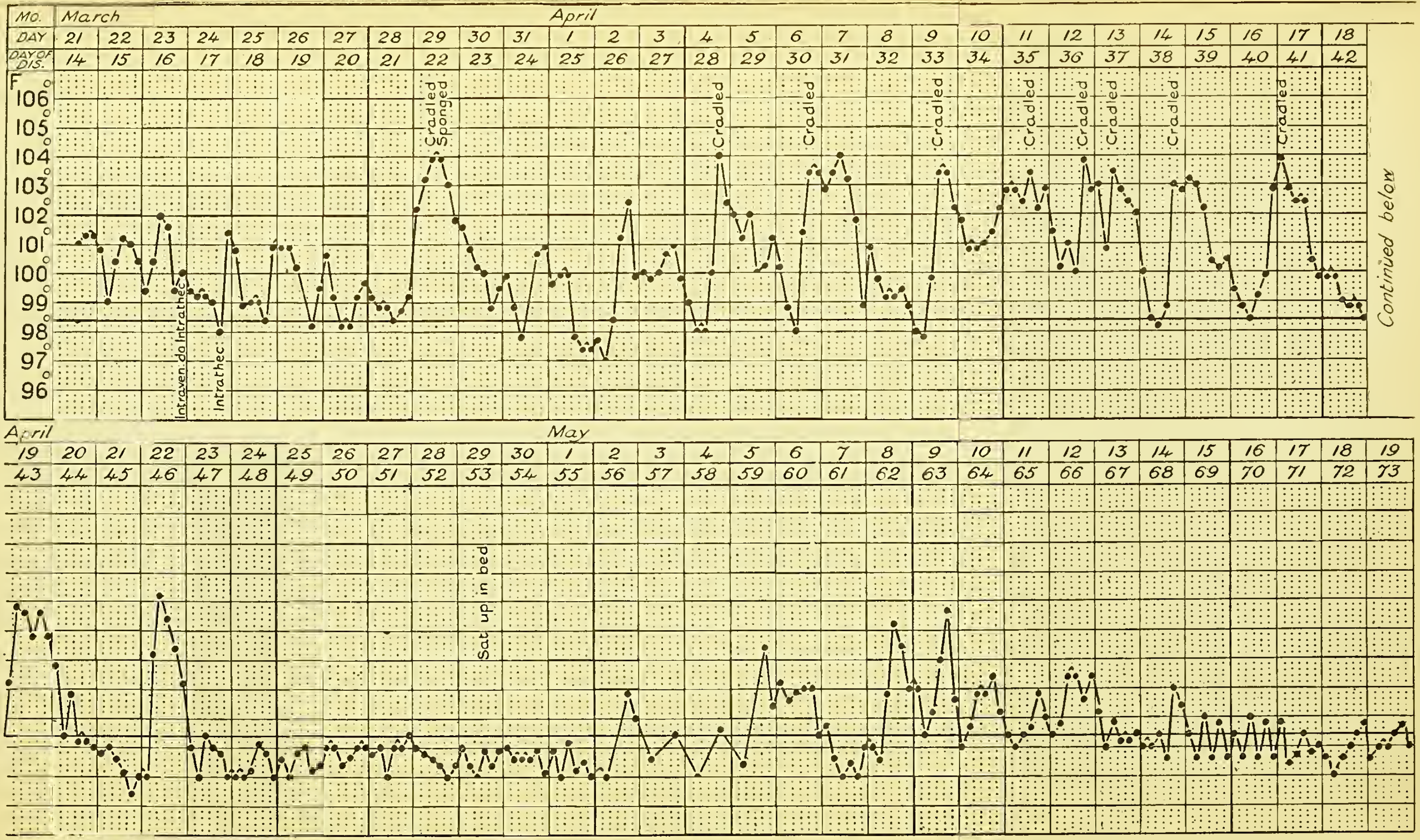

CHART 8.—The patient was a child, aged seven years, under the care of Dr. Garrod. Despite the frequent use of serum and the employment of lumbar puncture, the temperature continued unsatisfactory, and the patient's condition precarious until the 46th day, when sensitized vaccine was given. The result was at once good. A relapse occurred on the 56th day. More vaccine on the 66th day was again followed by marked improvement, which continued until convalescence was established. This chart also shows the sudden rise of temperature (22nd day) which commonly follows immediately upon serum administration, as well as the intermittent type of fever (38th to 46th day) frequently seen towards the end of the attack.

infection and hydrocephalus. This patient was under the care of Dr. A. E. Garrod, who kindly permits me to refer to the case. It will be noticed that upon two separate occasions the use of the vaccine was followed by a marked fall in the temperature, and that after the second fall it did not rise again. A dose of 20 million sensitized meningococci was given on the 39th day, 100 million on the 41st day, 500 million on the 43rd day, and 1,000 million on the 45th day. A relapse having begun on the 59th day, 500 million sensitized cocci were injected on the 65th day and 100 million on the 67th day. Convalescence appeared to be definitely established after the vaccine treatment.

Colebrook advocates the use of vaccine much earlier in the disease than the writer regards as desirable, naming the second or third day as a time when it should be exploited. This observer prefers, of course, to employ an autogenous vaccine when practicable, but suggests the use of a polyvalent stock preparation in times of epidemic. Colebrook's suggested doses are from two to five million in young children and from seven and a half to twenty million in adults ; these doses he repeats every third or fourth day. It is impossible at the present stage of our experience to estimate the true function of vaccine in the treatment of cerebro-spinal fever. The method calls for further trial and observations.

CHAPTER XIV

PROPHYLAXIS

THE preventive measures to be undertaken against the spread of cerebro-spinal fever can be considered in relation to the treatment of the patient, of the healthy carrier, and of the remainder of the community.

§ 1. **Isolation and General Management of the Patient.**—The principles governing these matters are those applicable to infectious diseases in general. Although it would appear that the healthy carrier is more responsible for the spread of the disease than the patient himself, it is none the less important to isolate every case of the disease and to exercise all precautions against further contact with healthy persons. Whenever possible the patient should be transferred to a hospital, and preferably to an institution where the staff is accustomed to dealing with infectious diseases. Reference has already been made to the necessity of choosing nurses trained in the proper care of the mouth and secretions. All bedclothes, towels, and utensils must be kept separately for the patient and must be properly disinfected after use. The stools and the urine must be mixed with some strong disinfectant prior to disposal. During his examination of the patient the physician should use a gown, and when taking throat swabs a mask is advisable. Before the patient is allowed to mix with other people his throat and nose must be proved to be free from meningococci. The special treatment of the naso-pharynx, described in the next section, should be resorted to in order to hasten the process of elimination of the coccus from this situation during the patient's convalescence.

§ 2. **The Treatment of the Carrier.**—All contacts who are found to be carriers should be placed under quarantine, and should be kept there until the naso-pharynx is free from meningococci. The carrier should live as far as possible in the open air. The naso-pharynx should be thoroughly washed several times daily, by sniffing up one of a number of solutions that have been advocated, and returning the fluid through the mouth. This is, for obvious reasons, more definitely indicated than gargles or throat sprays, although these may also be used. For the lavage of the naso-pharynx, and for a gargle, a weak solution of izal may be used, or peroxide of hydrogen, or a 1 : 1,000 solution of permanganate of potash, adding 1·5 per cent of sodium sulphate to assist penetration (Gordon). For spraying the nose or fauces a 1 per cent solution of iodine with 2 per cent of menthol in parolein may be used. The anterior nares may also be painted daily with the following preparation (Embleton and Peters) :

Ung. hydrarg. nit. dil.	ʒj.
Menthol . . .	gr. v.
Ol. olivæ . . .	ad ℥j.

Kolle and Wassermann suggested the insufflation of dried anti-meningococcus serum, and Kutcher considered that in eight cases so treated by him the results were very satisfactory.

The use of *meningococcus vaccine* for the purpose of clearing the throat of the coccus has not proved to be successful. There is no good reason why it should be. Similar negative results followed the use of Klebs-Loeffler bacillus vaccine in the analogous case of diphtheria carriers. If there is no interaction between a micro-organism and the tissues of the host it is difficult to see how, by a process of vaccination, any specific response can be elicited which could lead to the destruction of the bacterium.

In the case of most carriers, when treated as above recommended, the naso-pharynx is found to be free from meningococci after fourteen days, and in the case of the great majority in three weeks. It becomes an economic problem to decide how long to keep the more intractable carriers from their ordinary life. This important problem is more easy of solution under military than under civil rule. Indeed, the ideal measures with regard to the whole question of prophylaxis are those adopted under army regulations. As it is doubtless advisable for civilian authorities to get as near to this military ideal as is consistent with social obligations, it may not be out of place briefly to summarize the steps taken by R.A.M.C. officers whose duties lie in this direction :

'All cases of unaccountable headache, of apparent ptomaine poisoning, and of vomiting, with or without rise of temperature or pulse, as well as all cerebral cases, are isolated and notified. When the patient is diagnosed to be suffering from epidemic cerebro-spinal meningitis he is immediately sent to the isolation hospital, and not only his bedding but that of all his immediate neighbours is destroyed, and their blankets and clothing sent for disinfection. All the men sharing his room or hut are isolated from the first and kept under special observation for signs of the disease, swabs being taken from them by an officer deputed for the purpose. Not until these swabs prove to be negative is the house or hut pronounced free from infection, until when no man in it is allowed to return to duty. The isolation is real, for the men are drilled and paraded apart from the rest of their unit, and no direct intercommunication is allowed between them and the cookhouse, while all feeding utensils are swilled out with boiling water, and every man uses his own cups and plates. All waste matter is immediately destroyed by fire, special latrine arrangements are made for the use of contacts, and the systematic destruction of lice and fleas is undertaken, while samples of vermin are collected alive for investigation. Further, there is provision made for the isolation of carriers, through whose instrumentality, it seems certain, some of the outbreaks have arisen.' (*Lancet*, March 20, 1915.)

§ 3. **The Care of the Community.**—Prophylaxis for the healthy individual resolves itself into the use of general hygienic measures, with special reference to the avoidance of cold, catarrhal affections, and overcrowding. In epidemic areas schools should disperse and troops should leave barracks for roomy huts in the open air—provided, of course, in each case there is no incidence of the disease, nor occurrence of carriers amongst the individuals concerned. The billeting of soldiers upon civilians should cease. Coryzas and catarrhs generally should receive more attention than is usual. Specific inoculation is on trial, but in a somewhat desultory fashion. It is as yet impossible to say if such prophylactic inoculation is of service or not. Horder and Gordon found that very considerable protection was conferred upon rabbits by the intravenous injection of killed meningococci.

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